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SATURDAY JANUARY 14 1950

TABLE OF CONTENTS

Recent Work on the Virus Theory of Cancer C. H. ANDREWES, M.D., F.R.C.P., F.R.S. 81
Age of Puberty in the Tropics RICHARD W. B. ELLIS, M.D., F.R.C.P. 85
Hypersensitivity Reactions in Man HILDING BERGSTRAND, M.D. 89
Structure and Functions of Synovial Membrane D. V. DAVIES, M.B. 92
Birth Weight and Subsequent Weight R. S. ILLINGWORTH, M.D., F.R.C.P. 96
Comparison of Group and Individual Methods of Treatment A. S. THORLEY, M.D., D.P.M., and N. CRASKE, M.B., Ch.B. 97
Torsion of Omentum in Children A. BRUCE MACLEAN, M.B., F.R.C.S.Ed. 100
Stomach of the Recently Deceased A. WYNN WILLIAMS, M.D. 102
Diphtheria Immunization with P.T.A.P. in Adults TH. M. VOGELSANG, M.D. 104

MEDICAL MEMORANDUM
"Autemphysesis." PHILIP READING, M.S., F.R.C.S. 105

REFRESHER COURSE
The Early Diagnosis of Bronchial Carcinoma. R. C. BROCK, M.S., F.R.C.S. 116

GENERAL ARTICLES AND NEWS
Cortisone and ACTH: The Present Position in America J. W. MCNEE, M.D., F.R.C.P. 113
MEDICAL NEW YEAR HONOURS 115
LONDON'S HEALTH SERVICES 118
CHANGES IN NOTIFICATIONS 119
CYPRUS FREED FROM MALARIA 119
ORDER OF ST. JOHN OF JERUSALEM 120
NATIONAL FORMULARY, 1949 120
REPORTS OF SOCIETIES 120
UNIVERSITIES AND COLLEGES 133
MEDICAL NEWS 135
QUESTIONS AND COMMENTS 137

REVIEWS
Clinician's Guide to the Vitamins 106
Carcinoma of the Cervix 106
Portrait of Hurst 106
Static Diseases of the Legs 107
Books Received 107

OBITUARY
Clifford Dobell, M.A., SC.D., F.R.S. 129
W. H. Newton, M.D., D.SC. 130
Henry Corsi, M.B., F.R.C.S. 130
J. P. Buckley, M.D., M.S., F.R.C.S. 131
Neil MacVicar, M.D., D.P.H. 131
J. E. Lovelock, B.M., M.R.C.P. 132
A. Justina A. Wilson, F.R.C.P.Ed. 132
E. Hughes Jones, M.D. 132

LEADING ARTICLES
Shortage of Rh Testing Sera 108
Serum Cholesterol and Atheroma 109

ANNOTATIONS
Pertussis Vaccination and Encephalopathy 110
Antihistamine Risks 111
Hospital Contributory Schemes 111
Control of Biological Warfare 112
New Year Honours 112

CORRESPONDENCE
Fifty Years of Medicine. K. W. MONSARRAT, F.R.C.S.Ed.; J. M. RAPHAEL, M.D.; CEDRIC C. MECREDY, M.B.; WILFRED HARRIS, M.D. 121
Cancer Statistics. MALCOLM DONALDSON, F.R.C.S. 122
Silico-tuberculosis. H. MIDGLEY TURNER, M.D., and W. J. MARTIN, D.SC. 122

SUPPLEMENT
The Secretary Reports 3
Health Service.—CHANGES IN THE HEALTH SERVICE—ALLOWANCES FOR MEMBERS OF BOARDS AND COMMITTEES—GENERAL PRACTITIONERS IN HOSPITALS 6
HEARD AT HEADQUARTERS 7
QUESTIONS ANSWERED 7
PRIVATE PRACTICE COMMITTEE 8
GENERAL MEDICAL SERVICES COMMITTEE 9
FACULTY OF OPHTHALMOLOGISTS 10
AUSTRALIAN HEALTH SERVICE 10
CORRESPONDENCE 10
ASSOCIATION NOTICES 14

CORRESPONDENCE—*cont.*
Fate of the Foreskin. R. C. MACKEITH, D.M.; C. KILLICK MILLARD, M.D.; B. J. PECK, M.R.C.S.; E. GALLOP, M.D. 122
Infantile Gastro-enteritis Contracted in Hospitals. MARGARET N. DUNSTAN, M.B. 123
Reactions to Bee- and Wasp-stings. A. W. FRANKLAND, B.M.; HAROLD UPCOTT, F.R.C.S. 123
Parturition and Pneumonectomy. JUDSON T. CHESTERMAN, F.R.C.S. 124
Haematemesis due to "Disprin." C. JOSEPHS, M.B., and S. N. MATHUR, M.R.C.S. 124
Chilblains. E. F. W. MACKENZIE, M.B.; R. J. GOURLAY, M.D. 124
Authors and Psychopaths. R. A. HOEY, M.R.C.S.; I. GROSSMAN, M.R.C.S. 125
Weil's Disease. KENNETH ROBERTSON, F.R.C.P. 126
Diagnosis of Botulism. ALEX J. STEIGMAN, M.D. 126
Aureomycin in Treatment of Syphilis. R. R. WILLCOX, M.B. 127
Medical Administrators. CYRIL G. EASTWOOD, M.D. 127
Euflavine in Epididymo-orchitis. D. J. MACKINNON, M.B. 127
The Natural History of Asthma. L. E. WEAR, M.B. 128
Treatment of Wounded in Malaya. REX BINNING, M.R.C.S. 128
With Whales and Seals. E. T. EVERDELL, M.B. 128
Points from Letters 129

Epidemiology Section 133

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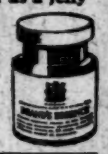

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THE BEARING OF RECENT WORK ON THE VIRUS THEORY OF CANCER*

BY

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Some neoplasms, for example a kidney tumour of leopard frogs and a series of sarcomata of fowls, own a virus as their causative agent. Filtrates of such tumours can be injected into other frogs or hens, as the case may be, and will reproduce histologically similar tumours in the inoculated species, and so on in indefinite series. With most animal tumours, however, filtrates are ineffective. It is supposed by what is called the virus theory of cancer that there is nevertheless only a quantitative difference between the fowl sarcomata and most new growths, that there are merely technical difficulties which prevent the filtration of, let us say, the propagable tumours of mice and rats, and that a virus is essentially concerned in the general run of cancers. The virus theory has had its ups and downs, mostly downs, for pathologists in general have not regarded it favourably. On the other hand, many bacteriologists, and particularly virus workers, are impressed by arguments in its favour.

A New Approach

The two Imperial Cancer Research Fund lectures preceding mine—that by Dr. Gye (1949) in March and that by Dr. Craigie (1949c)—have described a new approach to the problem in the Fund's laboratories. It seems possible that this work may open up a new chapter in cancer research. The College of Surgeons has asked me as a virologist to give this lecture, though I have not been personally concerned in cancer research for the last ten years. I have, however, previously worked upon and been deeply interested in the virus tumours for many years, and they possibly felt it would be useful for a virologist, standing on the side-lines, to say how the recent work struck him.

My own attitude to the virus theory is this: from the work of Rous, Gye, and others, and from my own, I have felt that there were very good reasons for exploring to the full the possibility that viruses caused all cancers. I have felt, for reasons I will explain, that the virus theory is intellectually satisfying. I do not consider it as proved, and am prepared to abandon it any day if shown good reason. I have just returned from the United States, where a reporter asked me my view on the virus theory. I replied that I thought it the best of the horses in the field, but that I would not, at this time, put my shirt on it.

The main reason for favouring the theory is that the virus is a good candidate for the post of a continuing cause of cancer. Bashford, Rous, and lately Gye, in his lecture last March, have ably pointed out how cancer must have both remote and continuing causes. *X* rays, ultra-violet rays, chemical carcinogens, can all act to incite the beginning of a cancer, which may thereafter be carried on in indefinite series by means of cell grafts. But, having started the cancer off, they cease to operate, and some other cause must be found for the continuing reckless growth of the tumour. Viruses are known causes of cell proliferation, which may be evident over considerable periods of time; so the continuing cause might be a virus.

Another continuing cause could be a somatic cell mutation, and this, taken in a broad sense, is the main visible alternative to the virus theory. It can be urged that to evoke a somatic cell mutation is to tell what we already know—that a permanent change has taken place in a somatic cell when it becomes cancerous; we thus get no further. This is a little unfair, for we do come a little nearer to visualizing a possible mechanism of the change, which must involve a biochemical modification of a gene. It can be urged with greater force that of the hundreds of mutations known to be possible in the germ-cells of the fruit fly *Drosophila*—where their study has built up a science of drosophilology—none is known to lead to cancer. On the other hand, agents which induce mutations, such as *x* rays and radium, are known carcinogens. As a weapon of argument this is two-edged, for what can induce mutation in a mammalian cell might also do so in a virus within that cell. Mutation of somatic cells in a mammal apparently is a rarity. Yet from the nature of things it might frequently happen to a cell with restricted powers of multiplication and never be observed. There is, however, one kind of mutation which would, if it existed, necessarily force itself upon our notice, and that is a mutation of somatic cells which led to unrestricted cell proliferation. The main objection to the somatic cell mutation theory of cancer is that it rests on pure speculation; there is no concrete evidence, as there is for the virus theory, that it has ever actually occurred and given rise to a cancer. Nevertheless some pathologists will continue to favour it, just as others will incline to reject it, until decisive evidence one way or another is forthcoming. The virtue of the recent Cancer Research Fund work is that it seems to offer a hope of deciding between the two alternatives of the continuing cause of cancer—an agent, most probably a virus, separable from the cell, or a change, a mutation perhaps, involving one or more genes, necessarily happening within a cell and not separable from the whole cell.

*An Imperial Cancer Research Fund Lecture delivered at the Royal College of Surgeons on November 29, 1949.

Before turning to this recent work I must explain in some detail why I describe the virus theory as intellectually satisfying. (I hasten, however, to say that what is intellectually satisfying to one pathologist is not necessarily true.) I have worked with viruses for more than 25 years, and the more I learn of them the more am I impressed with the variety of the virus–host relations which can be found. On the one hand are the viruses which attack, invade, and overwhelm their hosts in a matter of days or even hours: yellow fever and influenza and many other viruses can do this. At the other extreme is the bacteriophage in a lysogenic bacillus, causing no visible harm to its host and to be detected only by its power to multiply in and lyse some other species of bacterium—a so-called indicator organism—if this is presented to it. In the first case the virus multiplication goes on unchecked until so many essential host cells are killed that the host cannot survive. In the latter case the bacterial virus probably multiplies *pari passu* with the bacterial host, no faster and no slower, being carried along to each daughter cell as the host practises binary fission after the manner of its kind.

The causation of cancer could be but one of the numerous manifestations of host–virus relations. What properties would a virus have to possess to enable it to fulfil this role? It would have to be capable of inducing cell proliferation; it must, as we shall see, be very plastic and variable; it must be transmissible very early in life or even in the germ-plasm; it must normally exist as an inapparent or latent infection, being attuned to the rate of multiplication of its host cell so that it neither overgrows and kills it nor itself becomes overgrown and lost; it must be almost ubiquitous; it must be capable of being activated by an upset to the host–parasite equilibrium; it must be non-contagious in the ordinary sense. Let us consider these properties in turn and see whether they are known to occur among viruses.

Cell Proliferation

Apart from the viruses causing malignant tumours, such as that of Rous fowl sarcoma, many cause the cells they infect to proliferate for a time. Vaccinia does so, and so to an even greater degree does fowl-pox; but with them, as with most viruses, cell multiplication is inevitably followed by cell necrosis. Shope's rabbit fibroma produces massive swellings due to multiplication of fibroblasts, and might well pass for a sarcoma but for the fact that the lesions ultimately regress. While I would not urge that the Shope fibroma be considered a true neoplasm, it is worth mentioning that growths produced in ducks by fowl tumour viruses are also likely to disappear completely. The infectious warts of man, rabbits, and other species are innocent growths in which cell proliferation may continue for many months. Domestic rabbits can be infected with Shope's papilloma virus, though this is native to wild cottontail rabbits. In the tame rabbit, less often in the cottontail, the warts may fail to regress but continue to a malignancy which finally kills the animal with metastasizing growths.

The relation between the papilloma virus and the resulting epitheliomata is obscure: the virus infection certainly acts as a remote cause of the cancers, but the virus cannot be directly recovered from them—indeed, it may be impossible to obtain it even from the papillomata of which it is unquestionably the continuing cause. When the cancers are grafted into other rabbits, these develop neutralizing antibodies against the papilloma virus, thus showing that the virus is still present in the growths, perhaps in masked form. If, however, the grafting is continued long enough even this indirect method of detecting the virus's presence may fail. One can argue, quite reasonably, that the virus has disappeared and is therefore not the continuing cause of the cancers. It is, however, also possible that the timing between division of cell and division of virus has become perfectly synchronized, so that excess virus is no longer available to stimulate antibody production.

Variation

Viruses are so notoriously able to vary or mutate that this property needs little emphasis. One instance of this is the adaptation of a parasite of one species to growth in another—a plasticity of which virus workers take advantage every day; or the change in a virus to an affinity for one system, such as the central nervous system, instead of another—yellow fever and dengue viruses can be thus modified. Influenza virus is certainly capable of variation in its antigenic make-up. Of special interest is a change in the virulence of a virus for one and the same tissue. Thus the normal form of Shope's rabbit fibroma causes cell proliferation, but there is a variant which causes almost wholly inflammatory lesions (Andrewes and Shope, 1936). Probably the variant virus multiplies more rapidly and kills the cells instead of going along with and gently stimulating them, and the inflammation is the reaction of the tissues to the destroyed cells.

When we consider presently how various stimuli may upset a cell–virus equilibrium it will be obvious that a permanent change has often been induced by the upsetting stimulus. If the result should be a cancer, it would seem likely that the stimulus had acted by causing a mutation or variation of the hitherto latent virus or by so setting the stage that a particular mutant must emerge and dominate the scene.

One of the difficulties in the way of accepting the virus theory is a natural reluctance to believe that different histological types of tumour in different species can be due to different viruses, each causing a particular type of histological change in each kind of tissue of each species of animal. The number of cancer viruses necessary would be almost infinite. Fortunately such an imaginative feat is not required of us. One of the established facts of cancer research is that mammary cancers on continued transplantation may induce malignant transformation of their supporting stroma. It thus seems possible that there may appear a variant of an epitheliotropic virus having the power to infect connective tissue. There is also on record important work by Duran-Reynals (1942). He worked with the fowl-sarcoma virus of Rous, and this, in the fowl, is a stable virus, always producing tumours of the same general histological type with variations due merely to differing rates of growth. From chicks of a particular age group he was able to obtain Rous virus which could be adapted to grow in ducklings. The tumours he obtained were—and this is the important point—not all like the Rous fowl sarcoma, but showed considerable variation in histological pattern though all were connective-tissue tumours. Spontaneous duck tumours are almost unknown, so that the causation of Duran-Reynals's duck tumours can safely be attributed to the Rous virus. After adaptation to ducks it needed again a good deal of persuasion to induce the virus once more to infect chickens, and again some histological diversity was encountered. It seems as though when an established equilibrium is upset the virus may enter a plastic state. If such were the case one of the great objections to the virus theory would be overcome, for the

existence of infinitely numerous tumour viruses would not have to be envisaged.

Early Transmission

The virus of herpes simplex has been shown to be transmitted most usually to and from young children, giving rise to herpetic stomatitis. Those thus infected are commonly subject to herpes simplex or fever blisters in afterlife, but those who escape infection in childhood apparently acquire a measure of non-specific resistance and may never be infected at all. So, too, psittacosis infection is commonly acquired by baby budgerigars as a nest infection, persisting in a latent form and perhaps never causing any trouble (Meyer, 1942). The Bittner virus of breast carcinoma in mice is, as is well known, commonly transmitted to sucklings in their mother's and foster-mother's milk.

Such instances could be multiplied many times, but what is more important is to consider the possibility of infection of cells with a virus before birth. Such must surely happen with some tumour viruses if viruses are to be postulated as concerned in all tumours; for Rous was able to induce cancers of various sorts in *embryonic* tissues of mice by treating them with methylcholanthrene (Rous and Smith, 1945).

The virus of lymphocytic choriomeningitis is one known to be capable of infecting baby mice *in utero*; indeed, with one strain of mice Traub (1939) found that such infection was the rule, all mice born of the infected mothers having a latent infection. One may ask also whether the congenital abnormalities which occur in children whose mothers have rubella early in pregnancy may not be due to *in utero* infection with that virus.

If we turn to arthropods we find that the virus of St. Louis encephalitis is carried in or on the ovum in the chicken mite *Dermanyssus gallinae*—a fact which explains the mechanism, hitherto a mystery, by which it was carried along through the winter months. Viruses affecting caterpillars of certain moths are also thought to be carried in or on the ovum or sperm.

An interesting example is afforded by scrapie, a virus disease affecting the nervous system of sheep and causing them to itch violently, lose their wool by scraping against posts, and often ending in incoordination, convulsions, and coma. The incubation period of the disease after inoculation is two years. Apparently a so-called scrapie ram can transmit infection to his offspring, though these remain unaffected till 2 years old. The ewe, their mother, may remain unaffected and bear healthy lambs by another ram. Transmission by the sperm is indicated in this disease also. Congenital infection with a virus seems thus to be a known phenomenon.

Inapparent Infections

Latency of virus infection is also so frequent as to be a commonplace. When we know more we may discover that virus infections are latent more often than they are overt, just as saprophytic bacteria are far more numerous than pathogenic ones. We have already had occasion to mention several examples. Herpes simplex lies latent in a majority of human beings, lymphocytic choriomeningitis in all mice of certain stocks, psittacosis and related viruses in many colonies of budgerigars and pigeons; scrapie is latent in the scrapie rams. So, too, a plant virus is latent in every King Edward potato, and phages lie hidden as unsuspected inhabitants of many apparently normal bacteria—so-called lysogenic bacteria. The Bittner virus may be for ever concealed and harmless in the mice carrying it.

Ubiquity of Viruses

In many of the above instances—herpes, psittacosis, choriomeningitis, and the lysogenic bacteria and King Edward potato—the virus may be present in almost every individual of certain strains or stocks.

Activation of Latent Viruses

The equilibrium between latent viruses and their hosts may be upset in many ways, the result being manifest disease. An intracerebral injection of broth may produce lymphocytic choriomeningitis in a carrier mouse. Overcrowding and faulty management may produce a crop of psittacosis cases in the budgerigar colony. The stimuli which may bring out a crop of fever-blisters in a so-called "habitual herpeticker" are many and various: ultra-violet light, artificial heat, fever, and colds are among them. Chronic latent encephalitis may be set up in rabbits with herpes virus, and sublethal anaphylactic shock is particularly effective in activating this—a possible clue to the mechanism of the action of some of the agents effective in starting off herpes blisters in man. It is of some interest that Shope's rabbit fibroma—which is a benign and local though not exactly latent infection—is rendered much more active and becomes generalized when the infected rabbits are injected with tar or carcinogenic hydrocarbons (Ahlström and Andrewes, 1938). Time and experience will show whether this finding has any bearing on the power of carcinogenic chemicals to evoke cancers, whether in fact they can perchance be acting by upsetting an equilibrium between a tumour virus and its host cell.

Transmissibility

Whether or not cancer has a virus as a factor in its causation, it is certainly not an infectious or contagious disease. Neither are the acknowledged virus-tumours, the fowl sarcomata. Nor is herpes simplex in adults, or only very feebly so. Nor is St. Louis or equine encephalitis as it occurs in man or the horse. Nor is pseudo-rabies in cattle. Nor are any of the many virus diseases which are rare highly conditioned manifestations of a virus infection which is very widespread. Ready transmission of a virus disease happens very often, but often it does not.

It will now, I hope, be clear why I find the virus theory of cancer satisfying, for a cancer virus fits quite comfortably into the body of facts we already know concerning viruses and their varied habits. There is, however, the undeniable fact that the virus theory is only a theory and that it cannot be regarded as proved in face of an inability to find, in cancers in general, positive evidence for the existence of a continuing cause apart from the cell itself. Most transmissible tumours of mammals are *not* filterable like many fowl sarcomata, and have not hitherto been transmitted otherwise than by cell grafts.

Two Recent Lectures

In this context must be read, or have been heard, the two recent Cancer Research Fund lectures by Drs. Gye (1949) and Craigie (1949c). Here are definite suggestions that the widely studied cancers of mice may not, after all, be essentially different from the virus tumours but like them transmissible by means of something other than the living cell itself. Dr. Gye and Dr. Craigie will, I trust, forgive me if I act as devil's advocate and examine their evidence critically in order to determine whether or not we are in a position to regard the virus theory as being proved or

even substantially buttressed by the recent work. Their approaches are very different. Dr. Gye has long been an advocate of the virus theory and feels that recent findings finally establish its truth. The point at issue is, however, so fundamental in cancer research that the many who dislike the virus theory—and they are not necessarily diehards or fools—will require proof of unusual rigidity before they will accept his conclusions. Dr. Craigie's approach is more cautious: he is concerned to establish new and better quantitative methods for attacking the problem and eventually to see where this line of attack has brought him as regards the truth or falsehood of the virus theory.

The pith of the matter is whether mouse tumours can be transmitted by agents other than intact cells. Filtration would be the most certain method of proving this. But with viruses of low titre or great lability filtration may fail and recourse must then be had to other techniques. Dr. Gye raises the question of whether living cells can survive fine mincing and suspension in media containing glucose, whether they can withstand freezing and above all desiccation. As regards the freezing of suspensions of minced tumours, he writes: "The results cannot be interpreted simply as being the consequence of survival of cells on freezing"; and, again, "It is in the highest degree improbable that the tumours are a mere grafting of living cells." He admits that there is some doubt in the matter. Miss Mann (1949a), however, writes: "By freezing mammary carcinoma tissue at −79° C. for long periods the tumour cells are killed." Much evidence suggests that this is so, but many will feel that rigid proof is lacking. Miss Mann (1949b) finds that minced mouse embryo will form "large embryomas which persist for months or indefinitely" when grafted into homozygous mice. Such embryo-mince, unlike tumour tissue, is rendered ineffective by freezing. There are, however, no data on the relative dilutions to which embryo-mince and tumour-mince respectively can be subjected without loss of potency. There is not excluded the possibility that freezing reduces both alike by 99%. It is known that skin grafts can be kept frozen and used successfully. Craigie quotes Briggs and Jund (1944) in this connexion. Klinke (1937) claims to have obtained growth of tissue cultures from frozen tissue, though others have failed. To say the least, there is this conflict of opinion on how far freezing kills mammalian cells.

The dextrose which Craigie (1949b) uses to preserve his cell suspensions causes profound alterations in nuclear structure as seen with the phase-contrast microscope. One could be pardoned for presuming cell death when seeing such changes; these are, however, reversible when sodium chloride is added, so one is in doubt what to think.

All are agreed that a mammalian cell completely dried is much less likely to be alive than one frozen or treated with dextrose. Gye naturally regards experiments with dried tumour tissue as more conclusive than those where other methods of treatment are used. Craigie (1949a) has described the drying-plant which made possible the propagation of tumours with the aid of dried tissue, and his first successful results with a mouse sarcoma. He obtained, but has not yet published, quantitative information indicating the relative activity of the fresh and dried tissue.

Points on Drying

Accounts of successful drying of two other mouse sarcomata and three mouse carcinomata are less detailed as yet in that they lack such full quantitative data. The available evidence indicates that drying has been very complete, perhaps more complete than the standard lyophilization used by workers with bacteria and viruses. Three points, however, need comment. The drying has been done in most experiments in the presence of dextrose, the water of crystallization of which has not been removed, or of glycerin. Ignorance of what could happen to a cell dried in such circumstances introduces an unknown element into our appraisal of the results. Secondly, the dried tumours have as yet been tested immediately, without any storage in the dried state. Thirdly, in Dr. Gye's lecture and Miss Mann's paper (Mann and Dunn, 1949) much emphasis is placed on the use of a novel principle—the holding of tumour for some time in the frozen state before drying. The results certainly show better survival in the experiments where this was done—an unexpected and unexplained finding. The point may be as important as the authors believe, but the published data lack adequate evidence that the same tumour specimen dried after storage at −79° C. gave better results than when dried from the fresh state. More *ad hoc* experiments are necessary before the importance of the steps can be rightly evaluated.

The Histological Approach

Histological evidence indicates that the dried yet still potent tumour tissue contains no living cells. This, when cleared, embedded, and cut without rehydration, has an appearance very unlike that of living cells. True, the grosser cell-structure is largely restored on rehydration, but finer structure remains much impaired. The histological approach, however, has the grave disadvantage that an odd living cell here and there might escape the most careful observation. Most pathologists, asked whether mammalian cells could survive desiccation, would say "No," but others would reply "Why not?" particularly if the alternative was an admission that cell-free transfer of malignancy was established. Survival of dried bacterial cells is a commonplace, and, lately, spermatozoa have been found able to wiggle their tails after not quite complete drying in the presence of glycerin. Histology, argument, or preconceived ideas cannot settle the matter. The important question has to be decided by other means.

One obvious approach is to see whether a dried carcinoma will "take" when introduced somewhere where it has no access to the appropriate epithelial cells. An epitheliotropic carcinoma-causing virus would not be expected to produce tumours if it had access only to connective tissue: carcinoma grafts could of course, and commonly do, grow in such situations. If a dried carcinoma were able to grow in these circumstances, that fact would suggest that intact cells were still present. Unfortunately the most readily available mouse carcinomas are mammary growths, and mammary tissue is present almost everywhere in a mouse's subcutis. Rudiments are present even in males. Conclusive evidence would be likely to come from study of carcinomas of epithelium other than that of the mamma. Miss Mann (1949a) sought to settle this matter by injecting frozen mammary cancer tissue intraperitoneally, and finds that, while it takes well subcutaneously, it fails to take in the peritoneum except in odd instances. An occasional carrying-in of a little breast tissue on the needle is invoked to explain this—and not unreasonably. The unfrozen grafted tumour is reported to take both intraperitoneally and subcutaneously. Unfortunately, the experiment is inconclusive, for we are again not told at what dilutions the fresh and frozen tissues respectively would give takes by the two routes of injection. Without this knowledge we cannot interpret the result.

Grafts of the tumours so far studied by Gye and his colleagues grow best, or exclusively, in homozygous mice.

No details are yet available about whether the frozen or dried tissue is equally dependent for successful growth on being injected into a mouse of the same genetic constitution. If it were not, there would be good reason for thinking that cell-grafting was no longer wholly the mode of transmission. If it were still necessary, we should have to believe that we were dealing still with grafted cells or else with a virus having a novel type of specificity—not merely for a particular species, but for individuals within that species of a particular constitution; this would indeed be novel but by no means impossible.

I must mention in passing that some would like to reconcile the virus theory with other theories of cancer by supposing that an inheritable cellular change is always involved, but that in some exceptional instances, as in fowl sarcomata, a self-replicating piece of the altered cell, a plasmagene, or what-you-will, becomes free and able to affect other cells; that, in fact, a tumour virus when demonstrable is a product of the attacked cell and not an autonomous parasite. This to me is a hypothesis with almost nothing in its favour; it is gratuitously unnecessary. If there is a free active agent concerned, I prefer to think of it as an honest-to-goodness virus, an independent parasite like other viruses, and I have already tried to show that its properties would not greatly differ from those of other viruses. Heterogenesis, the doctrine that living things may arise from something utterly unlike themselves, as flies from putrid meat, has been propounded again and again; it has always proved wrong, and will again.

Conclusion

My lecture may have seemed to be arguing, as to its first half, for accepting as feasible the virus theory of cancer and, as to its second half, for doubting a lot of the evidence put forward in favour of that theory. That is not an illogical position. I confess that I should feel, if the virus theory were proved true, that the world was a more orderly place and that all was ready for important advances in the cancer field, going on from the newly consolidated ground. That is the very reason why I feel such an impelling need for confidence that the ground is truly solid and that this can never shift from under our feet. It would be of first-class importance to establish certainly that mouse cancers in general—and not one or two abnormal growths—could be transmitted otherwise than with intact cells. The new techniques Dr. Craigie has described open the way to settling this matter. There are so many things crying out to be done that I am sure we shall learn much more very soon. But—*festina lente!* If I cannot be very positive and dogmatic to-day, let it be remembered that I have been trying to review the present position of the virus theory at a very difficult time, when a new attack on the problem is just being launched.

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AGE OF PUBERTY IN THE TROPICS

BY

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The belief is widely held that children mature earlier in tropical than in temperate climates. This view has not only been repeated by medical authorities but in some instances is reflected in local legislation relating to age of consent and marriage and to the protection of juvenile labour. In actual fact, however, such evidence as exists points to a later rather than an earlier age of menarche (first menstruation) in girls living in tropical areas. No statistical studies of boys appear to have been made. Mills (1937), from a study of the mean age of menarche and the presumptive period of adolescent sterility following the menarche, states: "Sexual maturity in tropical countries comes fully two years later than in the most stimulating temperate regions."

While most recent studies have lent general support to Mills's view that in a tropical climate the menarche is retarded rather than accelerated (Howe, 1939; Ito, 1942; Kark, 1943), and Ogle (1934) has shown that a hot moist atmosphere may retard sexual maturity in experimental animals when the diet is controlled, it is clear that the available evidence is still rather meagre and much of it open to criticism. This is understandable when it is remembered that in many communities living in tropical areas knowledge of exact age is exceptional and memory of age of menarche correspondingly unreliable. It is also impossible in most instances to assess the relative importance of socio-economic conditions, including diet, and of climate when comparing subjects living in tropical or temperate regions. Heredity, on the other hand, whilst it may affect the age of puberty of the individual, is probably not of major importance when communities of different ethnic stock living under similar social and environmental conditions are compared (Hogben *et al.*, 1948; Michelson, 1944).

The following investigation was carried out in Nigeria during the rainy season, July to September, 1949, and comparisons made with figures previously obtained in Great Britain for both girls and boys (Ellis, 1947). The great majority of the subjects included in the study were children born and educated in Lagos, where births have been registrable long enough to allow verification of age; a smaller proportion were children from mission schools elsewhere in Southern Nigeria whose age was accurately known. None of the children had been out of Nigeria, and no European children were included. Although no attempt has been made to classify the children by tribes, the great majority were Yoraba or Ibo. Since school-children in Nigeria represent a privileged section of the community, it may be assumed that the nutrition of those included in the survey would be above the average of children in the southern provinces generally, where probably less than 20% of girls of school age are in fact attending school.

The Southern Nigerian diet is largely vegetable (yams, cassava, cornflour, plantains, etc.) and includes little meat and practically no milk. Fish, though expensive, is more readily obtainable in Lagos than in most inland areas. Red palm oil, which is widely used, provides a rich source of vitamin A and palm wine of vitamin B complex. A considerable number of the Lagos children were receiving a mid-day meal at school, which usually meant that groundnuts

and rice were included in the dietary. In only one group of 40 boys included in the survey was there evidence of widespread vitamin B deficiency, as shown by a high incidence of angular stomatitis; these boys were from a residential mission school where palm wine had been excluded from the diet. In general, the physique and nutrition of the children appeared reasonably good, despite a high incidence of latent malarial infection and the presence of intestinal parasites (principally ascaris).

The township of Lagos, which is situated on a coastal island in latitude 6° 27′, approximately 450 miles north of the Equator, has a characteristically tropical climate, though it is not so hot as some inland areas and has a lower rainfall than Calabar. Meteorological conditions are indicated by figures quoted from Quinn-Young and Herdman (1948): mean maximum shade temperature, 89° F. (31.66° C.); mean minimum temperature, 71° F. (21.66° C.); mean relative humidity, 79.5%; annual rainfall, 71.63 in. (181.87 cm.).

Methods

Since puberty represents a series of changes which include alteration of growth-rhythm, endocrine readjustment, and the appearance of secondary sexual characters, taking place over a more or less prolonged period, it follows that attempts to define and compare "the age of puberty" by any single criterion are at best arbitrary. The series of pubertal changes which occur have been discussed in more detail by Greulich *et al.* (1942), Hogben *et al.* (1948), and others. Nevertheless, comparisons between comparable groups made on the basis of clearly defined though restricted criteria are of some value if their limitations are recognized.

In the case of girls, the great majority of observers have confined themselves to defining the mean age of menarche (first menstruation), without recording the signs of puberty—e.g., early breast development or appearance of pubic hair—which commonly precede it, or considering the adolescent phenomena—e.g., irregular menstruation or ovulation, adolescent sterility—which may follow it. Where this criterion is used, as in the present study, it must be clearly emphasized that the age incidence of only one manifestation of puberty is being compared, and that no information is offered with regard to the age of attainment of full maturity. In the present study the age of menarche was determined by questioning 300 Nigerian girls aged 17 to 21, the results being shown as a distribution curve representing the percentage menstruating in each year of age. Comparison was made with the information received from 470 nurses in Great Britain, aged 18 years and over (the majority being in training and under 25), this being referred to subsequently as the English series.

Two objections may be raised to this retrospective method of obtaining information. The first, and most important, is that memory is unreliable and that this factor might affect the two groups unequally. This was evident in Kark's (1943) study of Bantu girls, in which she found that older girls tended to give a later age of menarche than younger ones. In the present instance, however, all the girls questioned had been at school at the time of menarche, and random cross-checking of the age given against the child's school class and the season at which menarche had occurred gave general confirmation of the stated ages. Co-operation of the school staff in confirming ages was enlisted, but it was not possible to interview parents. The second objection to the method is that the mean ages of the groups compared may affect the mean ages of menarche; thus if the survey includes age groups in which less than 100% of girls have already menstruated the mean age of menarche will be lowered. Cross-checking with a further sample, however, showed that the proportion of girls in the 17 to 18 year age groups who had not reached the menarche was so small that it could be disregarded, and the Nigerian and English series were therefore considered comparable for the present purpose. From the results obtained, both the mean age of menarche and the median age—i.e., the age at which 50% had menstruated and 50% had not—were calculated. These were found to correspond closely, as would be expected with a regular distribution curve.

In order to check the findings a further series of 250 Nigerian girls aged 8 to 18 were examined, and each yearly age group was divided into the percentage non-pubescent (pre-menarche, and showing no evidence of breast development), the percentage pubescent (in which early breast development was present but the menarche had not occurred), and the percentage adolescent (those who had reached the menarche). The age of menarche was determined in the case of the adolescent girls. The number who had reached the menarche by each successive birthday could then be calculated and expressed as a percentage of the total who had passed that age. From these figures the median age of menarche for the group was determined, and could be compared with the median age of menarche of the previous Nigerian series. This method, which was employed by Wilson and Sutherland (1949), has the advantage that in a considerable proportion of cases the menarche will have occurred within one or two years of the time of inquiry, and that the likelihood of error due to faulty memory is correspondingly reduced. It may be noted in this connexion that the menarche is an event of considerable importance in the life of the West African girl, and one unlikely to be readily forgotten.

In the case of boys there is no well-defined point corresponding to the menarche which can be determined retrospectively. The age of onset of puberty was therefore assessed by the examination of yearly age groups. The boys in each age group were graded as non-pubescent, pubescent, or adolescent, and the number of each grade shown as a percentage of the age group. The criteria for these gradings have already been described (Ellis, 1946), and were the same as those used for the control series in Great Britain. Briefly, the grading "non-pubescent" was given when pigmented pubic hair was entirely absent and genital development infantile; "pubescent" when pigmented pubic hair and/or early but incomplete genital development was present; and "adolescent" when both growth of pubic hair and genital development were well advanced. Admittedly the classification is arbitrary, since one stage of development passes gradually and not abruptly into the next, but it has been found in practice that the grading serves to distinguish three successive stages of maturity in the great majority of instances. A total of 333 Nigerian boys aged 9 to 18 were examined and compared with a control series of 662 examinations made in Great Britain.

Results in Girls

The figures for the first Nigerian series of 300 girls are shown in parallel with those of the English series of 470 girls, each being expressed as percentages of the total number in the series. The superimposed distribution curves (Fig. 1) show the later occurrence of menarche and the more limited spread of the curve in the Nigerian series. The mean age of menarche in the Nigerian series is 14.22 years and that of the English series is 13.73; the difference between the means is 0.49 year, with a standard error of 0.085. Thus the difference is 5.7 times its standard error

TABLE I.—*Percentage Reaching Menarche in Each Year of Age*

Group	Nigeria (300)	Great Britain (470)
9–10 years	0	0·6
10–11 ,, ...	0	0·9
11–12 ,, ...	1·0	7·5
12–13 ,, ...	8·7	19·1
13–14 ,, ...	32·7	30·6
14–15 ,, ...	35·3	27·4
15–16 ,, ...	20·0	8·5
16–17 ,, ...	2·0	3·6
17–18 ,, ...	0·3	1·3
18–19 ,, ...	0	0·4

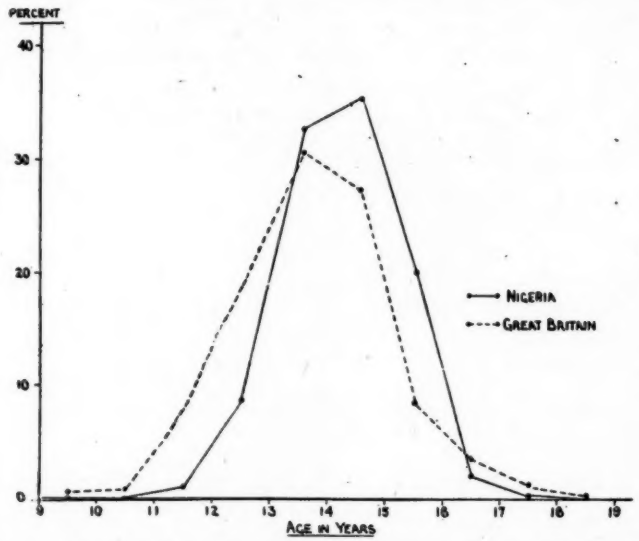

FIG. 1.—Distribution curves of age of menarche (Nigeria and Great Britain).

and may be considered statistically significant. The standard deviation of the English series is 1.37, while that of the Nigerian series is only 1.00, indicating a greater variability in the age of menarche in the English series.

The second Nigerian series was used for calculating the median age of menarche in order to cross-check the results in the first. Table II shows in parentheses the number who had passed each successive birthday and the percentage of these who had menstruated at that time. (The younger age groups have been omitted, since they are not relevant.) The corresponding percentages for the English control series and for Wilson and Sutherland's six Oxfordshire schools are given for comparison.

The median age of menarche in the second Nigerian series is 14.40 years. Although the numbers are small, this provides general confirmation of the findings in the first

TABLE II.—*Percentage of Children who have Reached Menarche at Each Successive Birthday*

Age	2nd Nigerian Series		English Control Series (Ellis, 1947)	6 Oxfordshire Schools (Wilson and Sutherland, 1949)
	No.			
11	(142)	0	1·5	1·0
12	(131)	0	9·0	7·5
13	(101)	12·9	28·1	29·6
14	(67)	37·3	58·7	63·3
15	(46)	69·5	86·1	89·4
16	(21)	85·7	94·6	95·4
17	(7)	100	98·2	98·2

Nigerian series, in which the mean and median age of menarche is 14.22 years. It will also be seen that the percentages in the English control series correspond closely with those given by Wilson and Sutherland, in whose series the median age of menarche was 13.6 years.

The percentages of Nigerian girls graded as pubescent in each year of age are shown graphically in Fig. 2. From this, the median age at which 50% were non-pubescent and 50% pubescent was 11.15 years—i.e., approximately 3.25 years earlier than the median age of menarche as calculated on the whole series. Although the numbers in each yearly age group are too small to be very conclusive they suggest a long time-lag between the earliest appearance of breast tissue and the menarche, assuming that the older and younger girls in the series had been living under similar conditions. In this connexion, Hogben *et al.* (1948) calculated by a logistic formula on a series of English school-

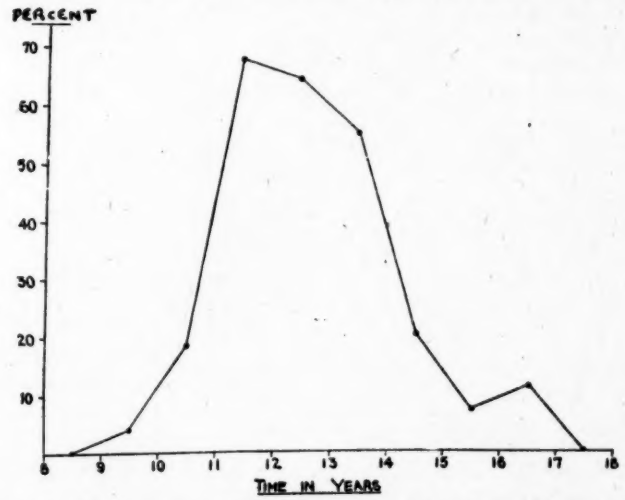

FIG. 2.—Percentage of Nigerian girls (second series) pubescent in each year of age.

girls that the age at which 50% were infantile with regard to breast development was 11.0±0.75 years, and with regard to menarche 13.6±0.77 years, a difference of 2.6 years.

Results in Boys

The percentages of boys graded as non-pubescent, pubescent, and adolescent in each year of age are shown in Table III, and the curves are compared in Figs. 3, 4, and 5.

TABLE III.—*Percentage of Boys Non-pubescent, Pubescent, and Adolescent in Each Year of Age*

Age Group (Years)	No.		% Non-pubescent		% Pubescent		% Adolescent	
	Nigeria	G.B.	Nigeria	G.B.	Nigeria	G.B.	Nigeria	G.B.
9–10	31	52	100	100	0	0	0	0
10–11	31	40	93·5	95	6·5	5·0	0	0
11–12	33	74	78·8	86·5	21·2	13·5	0	0
12–13	76	95	57·9	64·2	40·8	35·8	1·3	0
13–14	36	135	44·4	47·4	38·9	43·7	16·6	8·9
14–15	35	120	17·1	12·5	48·5	39·2	34·3	48·3
15–16	32	78	3·1	1·3	18·7	29·5	78·1	69·2
16–17	30	33	3·3	6·1	16·7	18·2	80·0	75·7
17–18	29	35	0	0	0	11·4	100	88·6

TABLE IV.—*Ages at which 75, 50, and 25% of Boys are Pubescent or More Mature*

% Pubescent or More Mature	Gt. Britain	Nigeria
75	14·14	14·10
50	13·14	12·95
25	12·15	11·80

It will be seen that the curves for Nigeria and Great Britain in Figs. 3–5 correspond more or less closely. In comparing the non-pubescent curves, it appeared best to take the median age (at which 50% of boys are non-pubescent and 50% pubescent or more mature), and also

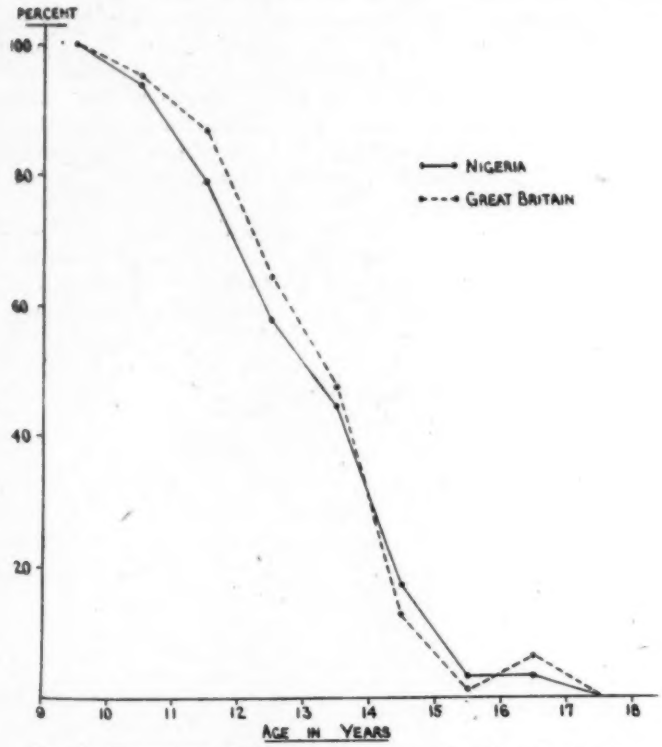

FIG. 3.—Percentage of boys non-pubescent in each year of age.

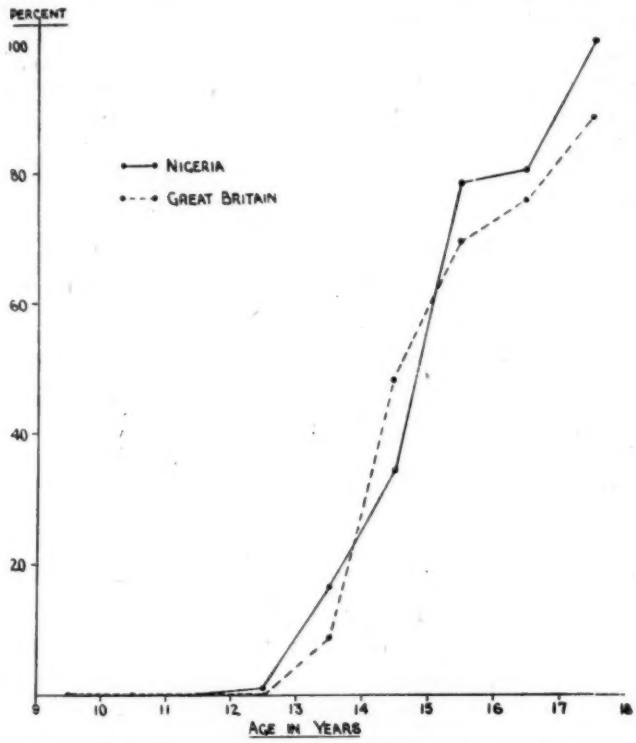

FIG. 5.—Percentage of boys adolescent in each year of age.

the ages at which 75 and 25% of boys are pubescent or more mature. The differences here are not statistically significant. There is also no significant difference between the two groups as regards the age at which adolescence is attained. In each case the median age is estimated at 15.0 years.

Summary and Conclusions

The above investigations lend no support to the belief that puberty occurs significantly earlier in tropical than in temperate climates. The mean age of menarche was found to be slightly but significantly later in Nigerian schoolgirls than in a control series in Great Britain. The mean age of menarche in this control series—13.73 years—may, in view of the regularity of the distribution curve, be compared with the median age of menarche of Oxford schoolgirls recorded by Wilson and Sutherland (1949), which was 13.6 years; a cross-check with a second series of Nigerian schoolgirls confirmed that the median age of menarche was later in Nigeria (14.4 years) than in Great Britain. The

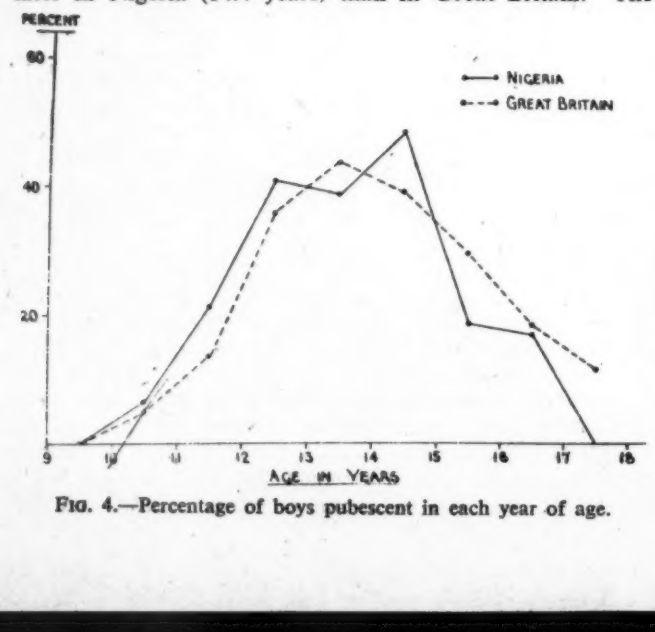

FIG. 4.—Percentage of boys pubescent in each year of age.

degree of maturity of Nigerian schoolboys of different ages was essentially similar to controls examined in Great Britain. In so far as the social and economic background of the Nigerian children included in the survey was better than that of the general population of Southern Nigeria as a whole, puberty might be expected to occur earlier in the children studied than in those living under less favourable conditions. It is not suggested, however, that the Nigerian series and the controls are closely comparable as regards diet, environmental conditions other than climate, or incidence of infection, and it is not claimed that any differences which have or have not been observed are attributable to climate alone.

The observations have, however, some practical applications. Thus the age of consent for an unmarried girl in Nigeria is at present 13 years, as compared with 16 years in Great Britain, whereas the mean age of menarche provides no support for this discrepancy. Nigerian law provides no protection against consummation of marriage before puberty, though a clear distinction should be drawn between "marriage by native law and custom," which is essentially a contract which may be made at any age, and consummation of marriage, which does not normally occur until after the menarche. Although native custom is strongly opposed to premature consummation of marriage, and it was in some tribes the custom for girls to enter a "fatting house" for one or more years after the menarche and before cohabiting with the husband, this prohibition is beginning to break down. With the drift to the towns, it is now not uncommon for children to reach the welfare officer in Lagos when marriage has been consummated before the menarche (Faulkner and Izzet—personal communication, 1949). Similarly, the Marriage Ordinance (as distinct from marriage by native law and custom) makes it possible for a child to be married at any age provided that the consent of her parents or guardian has been obtained. In a divorce case which recently came before the court, it appeared that marriage of a girl of 12 had

been effected by a Christian mission. While such cases are exceptional, they illustrate the danger of a belief in early maturity which appears to have no foundation in fact.

In the case of boys, legislation for the protection of juveniles in employment should be closely related to the expected development and physical performance at a given age (Ellis, 1948). In Nigeria this applies particularly to the minimum age at which boys may emigrate to Fernando Po for work in the plantations. In educational grouping and in defining regulations with regard to school-leaving age, it may well be borne in mind that adolescence is not likely to be reached significantly earlier in Nigeria than in Great Britain.

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THE PATHOLOGY OF HYPERSENSITIVITY REACTIONS IN MAN*

BY

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The title of this paper could have been "The Pathology of the Allergic Reactions in Man," but for reasons that will be evident later I consider it best to avoid the term "allergy." In his book on diseases of the liver Himsworth said of the term "cirrhosis" that it "not only misleads by implying an entity whose existence is doubtful, but has become so worn and defaced by loose usage as to have lost all precision." The same might well be said about the concept of allergy, which nowadays is used as a collective term for various forms of hypersensitivity. In characterizing a reaction as allergic we have said nothing about the precise nature of that reaction. For a better understanding of the character of allergic diseases, however, it will be necessary to distinguish between the various types of hypersensitivity reactions. I must therefore first give an introductory survey of the various forms of these reactions.

Anaphylactic Shock

A well-defined type of hypersensitivity is, as is well known, anaphylaxis. It is characterized by shock occurring when the antigen is injected into the circulation of the sensitized animal and by an immediate cutaneous reaction with weal-formation if it is injected into the cutis. The serum of the sensitized animal is precipitated by the antigen, and it is possible to transfer this hypersensitivity passively from one animal to another. The most important symptoms of anaphylactic shock are contraction of the smooth muscles and dilatation of the capillaries and smaller blood vessels. An anaphylactic reaction can be produced by a single injection of the antigen provided the dose is so large that sufficient antigen is left in the organism to react with the antibodies after their formation A reaction of this kind often occurs in human subjects who have been injected with horse serum for therapeutic or prophylactic reasons. We call it serum sickness, and the symptoms are temporary pains in joints and muscles, temporary swelling of the joints, erythema, urticaria, purpura, angioneurotic oedema, etc.

If we sensitize an animal by repeated intracutaneous injections of the antigen at regular intervals the local reaction becomes stronger with every injection and finally the swelling ceases to disappear, haemorrhages and necrosis occur, and ulceration follows. This type of anaphylactic reaction is called Arthus's phenomenon. The haemorrhages are a sign of severe damage to the vessels, and necrosis is a result of this damage.

The same symptoms that characterize experimental anaphylaxis and serum sickness also occur in many hypersensitivity diseases in men. In American literature these diseases are often described as "atopic" hypersensitivity reactions. As is well known, the prototype of these is pollen hypersensitiveness. One of the most prominent symptoms of anaphylactic shock is the contraction of the smooth muscles of the bronchi, where it is accompanied by dyspnoea. This symptom occurs in atopic hypersensitivity in the form of asthma. Besides the temporary cutaneous symptoms of serum sickness more chronic skin reactions sometimes occur in the form of eczema, particularly in children with hypersensitivity to food.

The antigen can be introduced by inhalation, through the digestive tract, or through the skin. This hypersensitivity is also transferable, as may easily be demonstrated by the Prausnitz–Küstner reaction. If the antigen is injected into the cutis there is rapid weal-formation as in anaphylaxis.

Drug Hypersensitivity

A special group of hypersensitivity reactions are those induced by a great number of substances of various kinds that are covered by the diffuse term "drugs." Many of these substances are not antigenic in themselves but become so only after having been conjugated with an albumin within or outside the body. These substances bring about two kinds of sensitivity reactions. The first is very like the atopic, the second more like the bacterial hypersensitivity reaction, which will be treated in greater detail later.

In the first type the sensitizing occurs through the respiratory tract, the digestive tract, parenteral injection, or epicutaneously, and the symptoms are similar to those occurring in serum sickness or in the atopic hypersensitivity diseases. In spite of this, however, it is usually not possible to produce an immediate reaction in the skin in the form of weal-formation by injecting the drug. Neither is it possible to demonstrate the hypersensitiveness to drugs by the Prausnitz–Küstner phenomenon.

According to Chase the difference in this respect from the previously mentioned hypersensitivity reactions is due partly to the fact that the quantity of antibodies in the

*A paper read in the Section of Pathology and Bacteriology at the Annual Meeting of the British Medical Association, Harrogate, 1949.

blood in drug hypersensitiveness is very small, and partly because it is not possible to perform a test with the antigen that produces the hypersensitiveness, as this antigen is formed only in the body. The latter difficulty, however, can be avoided, at least in certain cases, by conjugating the drug with an albumin *in vitro*.

In this connexion I would like to point out that in many cases the symptoms of hypersensitivity that occur in chemotherapy are not a reaction to the actual drug but a manifestation, provoked by the chemotherapy, of an already existing state of hypersensitivity. In these cases, therefore, the drug does not fill the role of antigen. The same is probably true of the great number of hypersensitivity reactions that have been observed in connexion with sulphonamide therapy. These reactions vary from mild symptoms like erythema and urticaria, or fairly serious symptoms like erythema nodosum and erythema exudativum multiforme, to very grave symptoms such as rheumatic pneumonitis and periarteritis nodosa. Several of my compatriots have proved that these symptoms often occur as early as one day after the treatment has begun, and consequently sensitizing to the drug in question cannot possibly have occurred.

The substances that bring about the anaphylactic type of drug hypersensitiveness can also produce a hypersensitiveness resembling the bacterial type. Clinically this type is manifested as contact dermatitis. Sensitization occurs through the skin, usually epicutaneously, and the clinical symptoms take the form of an eczema which appears when the sensitized skin is brought into renewed contact with the antigen. If the antigen is injected intracutaneously there is no reaction. If, on the other hand, the natural conditions are reproduced by the patch test there is of course a positive skin reaction. This reaction, however, does not appear immediately as in the atopic or anaphylactic type of hypersensitiveness, but only after 24 hours, like a tuberculin reaction or other hypersensitivity reactions of the bacterial type.

Haxthausen, in a series of very fine experiments, has established that the reaction is due to antibodies circulating in the blood. These antibodies cannot be transferred passively with serum. On the other hand Landsteiner, Chase, and Haxthausen have succeeded in transferring the hypersensitivity in another way. Landsteiner and Chase did this by means of suspensions of cells from peritoneal exudate produced experimentally in sensitized animals. Haxthausen did it by means of lymphocyte suspensions of thymus from sensitized animals: these were injected intraperitoneally into animals that had not been sensitized. Obviously the antibodies are in some way connected with the lymphocytes.

These facts provide a further resemblance between this type of drug hypersensitiveness and the bacterial type, which can be transferred in a similar way. Some investigations, however, also indicate a close relationship between the anaphylactic or atopic and the bacterial type of drug hypersensitiveness. Landsteiner and Jacobs have shown that certain substances give both a delayed and an immediate reaction, according to the way the antigen is introduced.

Bacterial Hypersensitivity

Finally, with regard to the bacterial hypersensitivity reaction, the prototype of which is the tuberculin reaction, it can, as is well known, be produced only by living or dead bacteria; but after sensitization the organism shows hypersensitiveness to the proteins of the bacteria in the form of a delayed reaction. If these proteins (for example, tuberculin) are injected into an animal it may be made to react anaphylactically, with an immediate skin reaction. However, the typical tuberculin reaction which appears after 24 hours is obtained only if we infect the animal with tuberculosis or, with some difficulty, if we inject dead tubercle bacilli into it. It is known that tuberculin hypersensitiveness cannot be transferred passively with serum, but, as I mentioned previously, Chase and several others after him have succeeded in transferring the hypersensitivity by exudate cells, chiefly mononuclear, from sensitized to unsensitized guinea-pigs. Kirschheimer and Weiser have obtained similar results with suspensions of spleen cells.

All the evidence points to a profound difference between the hypersensitivity of anaphylactic type and bacterial hypersensitivity, as the former reaction seems to take place only in the smooth muscles and the endothelium of the vessels, whereas the latter seems to affect all the cells of the body. Our knowledge of this problem has been greatly increased by the experiments of Rich and his collaborators.

In order to prove that the anaphylactic hypersensitivity reaction takes place in the endothelium of the vessels, rabbits were sensitized with serum in the usual way, after which the antigen was injected into the cornea. This has no vessels, but nevertheless it contains antibodies derived from the surrounding circulation. There was no effect. If, however, the cornea of the sensitized animals was damaged so that vessels grew into it, and the antigen afterwards injected close to the vessels, there was a strong reaction with haemorrhages. Other experiments demonstrated a quite different behaviour in bacterial hypersensitivity. If tuberculoprotein was injected into the cornea of non-tuberculous guinea-pigs there was only a slight reaction, whereas the cornea of tuberculous guinea-pigs treated in the same way showed marked changes and necrosis. Experiments with tissue cultures gave results which also support this theory.

It is clear, therefore, that a number of observations indicate a close connexion between the experimental anaphylactic reaction and some diseases in man. It may well be asked whether the pathological anatomy can give any support to the theory of such a connexion. This question must be unconditionally answered in the positive. The pathological anatomy of the anaphylactic reaction is now fairly well known, and damage to the endothelium of the vessels seems to be the most prominent change. In addition, very characteristic changes appear in the connective tissue. According to the theory held by Rich, that only the smooth muscles and the endothelium of the vessels are affected in anaphylaxis, the changes in the connective tissue ought to be secondary. There is, however, no conclusive proof that this is the case. All these changes are also found in various hypersensitivity reactions in man, as appears from works by Klinge, Laporte, Rich, and others.

Capillary Damage

The capillary damage has been described mainly by Rich. I would like to quote the following extract from his description of the capillary damage in rheumatic pneumonitis: "Focal necrosis of the capillary endothelium may occur, and the lumen may become plugged with a fibrinous or hyalin thrombus. Sometimes the capillary damage permits the occurrence of intra-alveolar haemorrhages. . . . Focal necrosis of the entire alveolar wall may occur where the capillary damage is severe. The lesions are decidedly focal, sometimes affecting only a segment of one capillary in an entire low-power field, though they often involve the vessels of a sufficient number of adjacent alveoli to produce confluent areas of consolidation." I would like to demonstrate a change of this kind (Fig. 1).

The section is from the lung of a 46-year-old woman who since the age of 15 had suffered from heart disease following scarlet fever. Three weeks before her death she became ill, with severe cough and dyspnoea. At the post-mortem examination mitral stenosis was demonstrated, with infarct-

FIG. 1.—Photomicrograph of foci in lungs showing characteristic changes of rheumatic pneumonitis.

like foci in the lungs. Microscopical examination of these showed changes characteristic of rheumatic pneumonitis with focal fibrinous thrombi in the heavily dilated capillaries and focal necrosis of the alveolar walls and some degree of intra-alveolar haemorrhage but very little exudate.

I have observed identical changes in the lungs of an old man who since childhood had suffered from various symptoms of hypersensitivity such as asthma, eczema, migraine, etc., and who finally died during an acute attack after he had been unconscious for 24 hours. This patient, however, also showed numerous pin-point haemorrhages in the white but not in the grey matter of the brain, which on microscopical examination appeared to be due to capillary changes that were in principle of the same kind as the ones I have just described and which are shown in Fig. 2. Here we see a small centre of necrosis surrounded

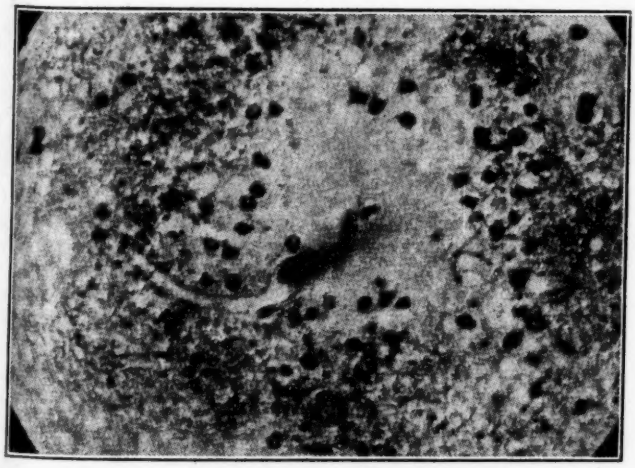

FIG. 2.—Photomicrograph showing pin-point haemorrhages in the white matter of the brain appearing to be due to capillary changes.

by a circular haemorrhage. A capillary runs through the circular haemorrhage and expands at the edge of the necrosis. Further along in the necrosis the wall is disintegrated and the lumen plugged by a fibrinous thrombus. The circular haemorrhage has naturally occurred because the capillary wall central to the thrombus has been so damaged that it has become permeable to red blood corpuscles.

Such capillary changes may be an explanation of the Arthus phenomenon, purpura, and, in their less pronounced forms, of erythema, urticaria, angioneurotic oedema, and swellings of the joints.

The changes in the larger vessels have, as we know, the character of periarteritis nodosa. It is here worth mentioning that Rich has produced periarteritis nodosa in rabbits by a single large dose of albumin. The most prominent changes in periarteritis nodosa are focal fibrinoid necrosis of the vascular wall, intramural and perivascular cell infiltration, and proliferation of the vascular endothelium which may sometimes be so pronounced that the whole lumen is plugged. Sometimes the proliferating endothelial cells take on the characteristics of giant cells.

If the above-mentioned theory is correct, that the vascular endothelium is the only organ directly affected in anaphylactic hypersensitivity, we must seek an explanation of the fact that the whole wall is damaged in this way in periarteritis nodosa. Here a theory presented by Schürman, MacMahon, and Doljansky to explain the vascular changes in malignant hypertension may be applicable. It is known that the vascular changes in malignant arteriolosclerosis are also characterized by focal fibrinoid necrosis rather similar to the changes in periarteritis nodosa, which has induced some writers to assume that arteriolosclerosis also may be a hypersensitivity reaction. There is hardly any difficulty in distinguishing between these vascular changes histologically—anyway, in the human subject—as the inflammatory cellular infiltration in and around the wall is lacking or very insignificant in arteriosclerosis. The writers I have just mentioned are, however, of the opinion that the fibrinoid necrosis of the wall in arteriolosclerosis is due to damage of the vascular endothelium which serves as a "Blutgewebeschranke." They consider that if the blood comes into immediate contact with the tissue a necrosis occurs.

Connective-tissue Changes

The changes in the connective tissue in man have been studied primarily in cases of polyarthritis rheumatica, and are therefore often termed "rheumatic." They are characterized by oedema and by focal splitting up of the collagen fibres into reticulin fibrils with changed colour reactions. They are coloured black by silver, whereas connective-tissue fibres take on a brown colour. Furthermore, the fibrils show positive fibrinous stain. The next step in the development is the fragmentation of the fibrils with proliferation of the fibroblasts around the centre of disintegration. Thus rheumatic granulomas occur, one type of which is the so-called Aschoff body. Finally a scar may be formed. The changes in the connective tissues may be very transient, but they may also remain for months or years.

All writers agree that these changes are localized to different organs in a way that seems quite capricious and that the changes within these organs are of a markedly focal character. Little is known of the reasons for this, but investigations made by Hawn and Janeway indicate that the nature of the antigen involved may play a part in determining which organ is affected. By sensitizing rabbits with pure serum albumin they obtained vascular changes similar to periarteritis nodosa, but only in some of the

animals. If, on the other hand, pure gamma globulin was used glomerulonephritis was the most prominent change in nearly all the animals.

The capricious localization is expressed clinically by the many forms of disease in man that seem to be hypersensitivity reactions of the kind I have just described, such as polyarthritis acuta, endocarditis, pancarditis, periarteritis nodosa, arteritis temporalis, rheumatic pneumonia, transient infiltration of the lungs, glomerulonephritis, lupus erythematosus disseminatus, Liebman–Sachs disease, urticaria, angioneurotic oedema, migraine, etc. These diseases, however, may also occur in numerous combinations. It happens sometimes, however, that so many of these so-called diseases appear simultaneously in the same person that it is doubtful how the case should be designated.

Thus, whereas the anaphylactic type of hypersensitivity reaction, at least in its most advanced form, presents a characteristic pathologico-anatomical picture, this is by no means true of the bacterial hypersensitivity reaction, as it appears, for instance, in the tuberculin reaction, which resembles an ordinary inflammation.

With regard to contact dermatitis, the pathological anatomy is of no help whatever in deciding whether this is of anaphylactic or bacterial type. For long there has been controversy on whether the changes are primarily localized to the epidermal cells or whether they are secondary to changes in the capillaries of the cutis. Haxthausen has recently made experiments that support the latter assumption.

Erythema Nodosum

Finally, in order to show the importance of distinguishing between the various hypersensitivity reactions, I would like to say a few words about a disease which has traditionally interested Swedish research workers—erythema nodosum. In 1921 Ernberg coined the slogan that erythema nodosum is the body's own tuberculin reaction. This statement contains two important assertions—first, that erythema nodosum is always caused by tuberculosis; secondly, that erythema nodosum is a hypersensitivity reaction of the bacterial type. The former declaration has been strongly opposed and successfully refuted. We know now that erythema nodosum also occurs in connexion with lymphogranuloma inguinale, streptococcal infections, etc. Little interest has, however, been taken in the latter assertion, though it has in general been accepted. But it might also be possible that erythema nodosum is a hypersensitivity reaction of anaphylactic type.

This view is not unreasonable. Already in 1929 Tillet and Frances showed that patients who are convalescent after pneumonia may show an immediate reaction to the carbohydrate component of the pneumococcus and a delayed reaction, similar to the tuberculin reaction, to the protein component. It is also known that an anaphylactic reaction can be produced by the carbohydrate component of the tubercle bacillus. Thus it is possible that in a tuberculous infection we have two parallel sensitizations—one to the protein component of the tubercle bacillus which results in bacterial hypersensitivity and is manifested in the tuberculin reaction, the second an anaphylactic reaction to the carbohydrate component of which erythema nodosum is an expression. That erythema nodosum often occurs when the tuberculin reaction becomes positive would then only mean that it takes approximately the same time for the two kinds of antibodies to form. This rule, however, is not quite without exceptions, for sometimes erythema nodosum occurs before the positive tuberculin reaction.

The clinical symptoms of swelling of the joints, urticaria, etc., which sometimes accompany erythema nodosum give additional support to this theory.

In my opinion the pathological changes in erythema nodosum also point in the same direction. For in the subcutaneous fatty tissue we find fibrinoid degeneration of the interstitial connective tissue, as has recently been shown by Wahlgren and Löfgren, and sometimes also vascular changes of the periarteritis nodosa type. I have myself had an opportunity of demonstrating this.

This question can naturally be solved only by testing patients suffering from erythema nodosum with partial antigens from tubercle bacilli and streptococci in order to find out whether they show any immediate reaction against these antigens. Strangely enough, investigations of that kind do not seem to have been made.

Finally, I should like to stress the importance of correlating our clinical, serological, and pathologico-anatomical knowledge of these problems better than in the past. The theory that the great number of clinical entities that I have mentioned here are only anaphylactic tissue reactions would then perhaps not be relegated to the world of fancy, as now quite often happens.

THE STRUCTURE AND FUNCTIONS OF THE SYNOVIAL MEMBRANE*

BY

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A thorough knowledge of the structure, nature, and functions of the synovial membrane is essential both for an understanding of the normal functioning of joints and for the interpretation and assessment of the changes which occur in disease. Despite the undoubted importance of this topic, knowledge of it is still to a great extent rudimentary. The literature is full of conflicting statements and is lacking in original observations, while textbooks on physiology in general tend to shun the problem. It is not intended to give here a comprehensive review of the subject, but to discuss some aspects in the light of my experience over the past twelve years. A few of the major problems remaining unsolved are raised in the hope that further investigation will be encouraged.

Development

The synovial membrane is the last of the joint tissues to be fully differentiated, and, as compared with the capsular structures and the skeletal elements, it is the least specialized, as shown by the frequency with which it is the source of heterotopic chondrification and ossification. The skeletal elements first take the form of mesodermal condensations (precartilage), which in turn are converted into cartilage and ultimately bone. Between the chondrifying skeletal elements is undifferentiated mesoderm—the so-called interzonal mesoderm or articular disk marking the site of the future joint and limited externally at an early stage by a cuff of condensed tissue delineating the capsular ligaments. Proximally and distally this capsular condensation blends with the more tardily differentiated perichondrium and later periosteum clothing the skeletal elements.

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The chondrified skeletal elements expand and grow both by proliferation of their constituent cells with the accretion of matrix among them—the so-called interstitial method of growth—and by a new deposit of cartilage at their surfaces, the mesoderm here proliferating and transforming through a stage of precartilage to cartilage. At this stage the enveloping layer of precartilage is characterized by the density of its nuclei and its avascularity. The more peripherally placed mesoderm is a reticulum later destined to be the osteogenic layer of the periosteum. The fibrous layer of the periosteum later limits this externally and is from the first continuous with the capsular ligaments. At the ends of the skeletal elements and over the future articular surfaces the precartilage and cartilage are derived from the interzonal mesoderm. Between the articular surfaces this remains avascular, whilst the more peripheral portions between the capsule and the intra-articular parts of the skeleton are early and profusely vascularized (Haines, 1947). The synovial membrane is developed from this vascular mesoderm, and its rich capillary bed remains one of its most distinctive features. The central parts, and later the more peripheral of the interzonal mesoderm, cavitate to form the future synovial cavity of the joint (Fig. 1). This

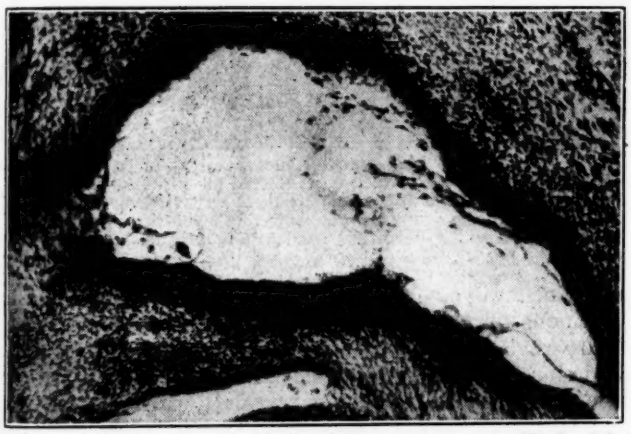

FIG. 1.—Section through the developing temporo-mandibular joint of a human embryo to show the process of cavitation to form the synovial cavity. (× 120.)

is achieved by enlargement and confluence of the meshes of the reticulum by retraction and detachment of its constituent protoplasmic bridges, thus allowing adjacent spaces to unite and form a composite large space. Liquefaction of tissue plays a minor part in the process, but cannot be excluded. A few cells become free in the joint cavity and constitute the first cellular elements in the synovial fluid. Cavitation is often incomplete in these early stages and may continue even into post-natal life. Thus, of the original mesoderm of the interzone, that over the articular surface and intracapsular regions is converted into cartilage, while more peripherally the vascular layer continues as the synovial membrane lining the capsule and the intracapsular parts of the skeletal elements. The intra-articular ligaments are also developed from this mesoderm, and are delineated even before cavitation begins.

The major synovial folds of joints such as the infrapatellar pad in the knee are mapped out as cavitation proceeds, although we are ignorant of the time and method of deposition of the fat.

Villi are absent in the earliest-formed synovial membrane; they do not represent tags resulting from imperfections or irregularities of the process of cavitation. They arise by proliferations of the synovial membrane and not by delamination from its surface. A few villi are present at birth; they continue to increase in number throughout life (Bennett, Waine, and Bauer, 1942).

Thus the significant features in the development of the synovial membrane are its slowness in attaining full differentiation, its early and pronounced vascularity, and the continuity of its parent tissue with chondrogenous tissue and later the osteogenic layer of the periosteum. The precocity of development and richness of the vascular bed denote its importance in the nutrition of the joint tissues, whilst its tardy differentiation and its genetic relation to cartilage and bone explain the frequency with which it is the site of heterotopic bone and cartilage formation. The marginal osteophytes of osteoarthritis develop in the region of transition and instability at the articular margin. Cartilaginous and bony loose bodies may arise in any portion, the latter either by ossification in cartilage or directly as intramembranous ossification without the intervention of cartilage. Indeed, cartilaginous and bony nodules may arise together in the same synovial membrane and in close proximity (Fig. 2) When detached into the joint cavity as loose bodies these nodules remain enveloped in synovial cells, which may continue to proliferate cartilage, or more rarely bone, so that in time they may become very large.

FIG. 2.—Section of the synovial membrane from a human hip-joint showing the formation of bony and cartilaginous loose bodies in close proximity to each other. (× 35.)

Components of the Synovial Membrane

The synovial membrane as a whole varies considerably in its appearance from one part of the joint to another. Key's (1932) classification of the types as areolar, fibrous, and fatty adequately represents this range of variation The fibrous type is in general thin and is placed directly on the ligaments of the joint, while from the physiological standpoint the loose areolar areas seem most active.

The Synovial Cells

Much discussion has centred on the nature of the synovial cells, their function, and their similarity or otherwise to the lining cells of serous cavities such as the pleural and peritoneal. They have been variously termed endothelial, mesothelial, and even epithelial. Some maintain that they differ little if at all from the underlying fibroblasts. Willis (1948) speaks of synovial fibroblasts at the surface of the membrane, merging without clear line of demarcation into collagen fibroblasts deeply, and at the articular margins showing transitions between typical synovial fibroblasts and cartilage cells. Key (1925) maintains that after synovectomy the new lining is re-formed by metaplasia of the underlying connective-tissue cells. These views are not wholly in accord with other observations. Unlike the lining of the serous cavities, these cells are irregular and ill-apposed; nevertheless in most histological preparations they differ from the underlying tissues by their depth of staining. With Mallory's connective-tissue stain they are characteristically coloured pink, whereas the

underlying cells are blue. Like peritoneal cells, they prevent adhesions between apposed surfaces. Such a function could not be attributed to fibroblasts. To what extent adhesions occur after synovectomy it is difficult to tell. Like peritoneal cells, they react to irritation by becoming rounded and enlarged and by multiplying. Few synovial cells appear in either the normal or the pathological synovial fluid. Their characters here are adequately described by Collins (1936) and others. They and the other cellular elements in the fluid are most conveniently observed in films fixed wet for 20 to 30 minutes with Schaudin's or Bouin's fluid and then stained with Giemsa's stain or iron haematoxylin. Alternatively, the synovial fluid may be poured into Susa fixative, when the mucin is precipitated, enmeshing the cells. The coagulum thus obtained can be treated like other solid tissues, dehydrated, embedded in paraffin, sectioned at about 5 μ, and then stained on a slide by the usual histological methods. I have outlined these methods because of their simplicity and convenience as permanent preparations.

Though the synovial cells are almost certainly the main, if not the only, source of synovial mucin, they do not stain metachromatically with such stains as toluidine blue or cresyl violet as do many mucin-secreting cells. The essential component of the synovial mucin, the hyaluronic acid, does not possess this staining property. A few metachromatically staining cells can be seen in the synovial membrane; these are always placed more deeply, and lie close to the blood vessels. They are mast cells (Davies, 1943).

In connexion with the nature of the synovial cells, the work of Vaubel (1933) merits special mention, and could be repeated and extended with advantage. According to that author synovial cells are distinguishable in tissue culture by their ability to liquefy the protein coagulum on which they grow—presumably secreting a proteolytic enzyme—and by their ability to secrete a mucin-like substance. Furthermore, their characteristic appearance in certain so-called synoviomata, and their ability to secrete a mucin here, point to them as the source of this substance and distinguish them from ordinary fibroblasts.

In addition the synovial cells have other important functions. They are active in the removal of particulate matter from the joint cavity and its transfer to the deeper tissues. Following haemorrhage into the joint cavity they are often loaded with haemosiderin. Routine examination for this pigment reveals its frequency, particularly in association with loose bodies in joints (Fig. 3). Large accumulations of haemosiderin frequently occur in the synovial cells also in villo-nodular synovitis, an inflammatory condition often erroneously termed xanthoma. Similarly, these cells probably participate in the removal of fibrin from the joint cavity in disease. Fibrinogen does not occur in normal synovial fluid but is often seen in pathological conditions. Interesting in this respect are lesions found in the metatarsophalangeal joints of cattle three weeks after the intravenous injection of the vole bacillus vaccine (Young and Paterson, 1948). The animal is pyrexial, lame, and off its food; the joint becomes hot, swollen, and tender. At this stage the synovial membrane is swollen, oedematous, and hyperaemic, and the synovial cells are enlarged and increased in number; the fluid in the joint is also increased and shows a high cellular content predominantly polymorphonuclear (Fig. 4). Fibrinous loose bodies are numerous and the surface of the synovial membrane is generally covered with a fibrinous membrane. The connective tissue around the blood vessels is degenerated and stains deeply eosinophilic. The lesion improves towards the end of a week, and examination after clinical recovery reveals a perfectly normal synovial membrane; the connective tissue is again normal, the synovial cells have returned to the usual size and arrangement, whilst the fibrin deposits have vanished, leaving no suggestion that they have become organized or incorporated into the membrane (Davies, 1948). The fibrin has presumably been lysed and absorbed. Vaubel (1933) notes the fibrinolytic properties of the synovial cells in tissue culture. This emphasizes the importance of the synovial cells in maintaining the joint fluid free not only of colloidal and particulate matter but also of extraneous protein.

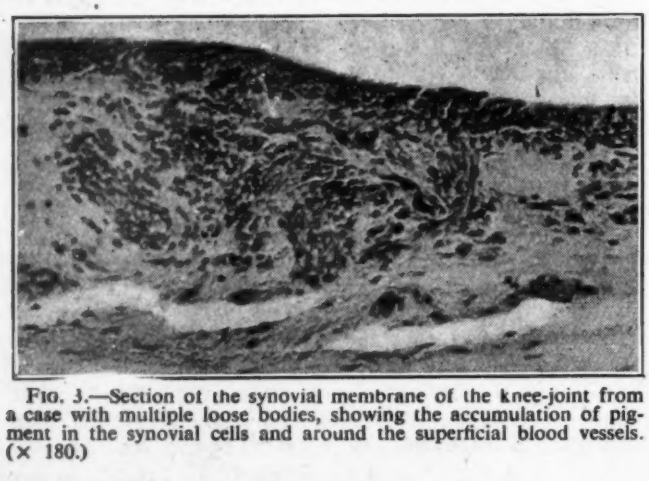

FIG. 3.—Section of the synovial membrane of the knee-joint from a case with multiple loose bodies, showing the accumulation of pigment in the synovial cells and around the superficial blood vessels. (× 180.)

FIG. 4.—Section of the synovial membrane from a metatarsophalangeal joint of an ox which had received an intravenous injection of vole bacillus vaccine approximately three weeks previously. Note the reaction of the synovial cells and the layer of fibrin on the surface. Most of the fibrin has been lost in preparing the section. (× 300.)

Villi; Fat Pads

It would be appropriate at this stage to consider the villi of the synovial membrane. As a rule more highly developed in other animals than in man, they have been shown by Bennett, Waine, and Bauer (1942) to become more numerous with age. Their overgrowth in certain pathological conditions is truly astounding. They have been variously held to be the source of synovial fluid and concerned in the removal of particulate matter from the joint cavity. Frequently, however, they are avascular, and as regards the removal of particulate matter do not compare in activity with the areolar areas of the membrane. What, then, can their function be? They increase the surface area of the synovial membrane, and possibly assist in maintaining the joint free of extraneous protein and allied substances. As yet, however, no close relation has been shown to exist between the capacity of the joint or surface, the volume of synovial fluid, the area of the articular surfaces, and the

area of the synovial membrane. The data available are too scanty for any definite conclusion to be drawn.

Likewise, to the fat pads, almost universally present, have been ascribed a variety of functions—secretion of synovial fluid, filling of dead space, distribution of synovial fluid, and action as pad oilers. They are relatively inactive in regard to both absorption from the joint and the secretion of synovial fluid. There is little in the way of precise and authoritative information about this fat in the chronic wasting diseases or in purely arthritic lesions.

Other Cellular Components

Concerning the other cellular components of the synovial membrane, Kuhns and Weatherford (1936) have drawn attention to the reticulo-endothelial elements. Subcutaneous injections of trypan blue in animals lead to a considerable deposition of the dye in cells at or close to the synovial surface but excluding the fat pads. The storage of dye is not so marked as in sites, such as the liver, spleen, and bone marrow, known to be rich in reticulo-endothelial tissue, and it is increased by inflammation. Those authors suggest that these cells are of importance in the localization not only of known bacterial infections but also of bacterial toxins and metabolic products. The distribution of gold following chrysotherapy maintains the pattern described above: it is then present in the synovial membrane in smaller concentration than in liver and kidneys but greater than in muscle, and in greater concentration in arthritic joints than in normal synovial membrane (Davidson, 1948).

Though the collagen fibres of the membrane are of the utmost importance in the pathology of joint lesions, little that is certain can be said of their development and behaviour in normal tissue. The development and fate of the elastic fibres under varying conditions still require investigation. They protect the synovial folds from being nipped between the joint surfaces in the various movements of the joint.

Apart from its richness, already noted, the capillary bed of the synovial membrane is superficially placed, and around the articular margin forms the anastomosing fringe of capillary loops of the circulus vasculosus (Fig. 5). This is directly concerned in the nourishment of the peripheral portions of the avascular articular cartilage, the more central portions of which are nourished indirectly through the synovial fluid (Fisher, 1923). Apart from its mucin, this fluid is now believed to be a dialysate of the blood (Bauer, Ropes, and Waine, 1940). The capillary bed is also the chief site of absorption of solutions, and, to a smaller extent, colloidal particles from the joint—the less conspicuous lymphatic bed with its rectangular pattern and lacunae playing a more minor part (Adkins and Davies, 1940). As would be expected both from the structure of the synovial membrane and from its profuse vascularity, oedema of the looser areolar areas is a frequent feature in disease. Small haemorrhages and even thromboses are also often seen here, whilst the multiple terminal capillary loops help to determine the localization of infection.

FIG. 5.—Human synovial membrane from the knee-joint showing the blood vessels of the circulus vasculosus. These nourish the peripheral parts of the articular cartilage and also the cartilage and later bone of the epiphysis. (× 27.)

Innervation

Finally the problem of the innervation of the synovial membrane constitutes one of the most controversial aspects of the whole topic. In this connexion the work of Gardner (1942, 1944, 1948), upon which I have drawn freely, needs special mention. Many conflicting statements appear in the literature: some describe nerve nets and even specialized nerve endings in the synovial membrane; others deny their existence. The nerves are few and always follow the blood vessels, close to which they terminate. No free nerve endings occur except in association with blood vessels and no complex end-organs are found (Gardner, 1948). My own more limited observations are in agreement with those of Gardner. This at once raises the question of the sensations arising in the membrane. In its looser and fatty areas it could hardly be expected to be concerned in the postural sensations. Is the membrane sensitive to pain, to touch, or to pressure? I have once had the opportunity of testing this in a patient with a subacute infective lesion: touching the membrane produced no response, nor did pricking with a needle, nor pinching with forceps. Tugging on it, however, was sharply resented, though the pain was poorly localized. This pain may have been mediated through nerve endings situated in or close to the capsular ligaments. The mediation of pain sensations along fibres, presumably of the autonomic nervous system, situated on the blood vessels, is also a possibility. While, then, the synovial membrane is of the greatest importance from the point of view of nutrition of the joint, the part played by it in the symptomatology of disease is open to question. Engel (1941) has reported somewhat paradoxical results from division and stimulation of the sympathetic supply to perfused joints, the former apparently decreasing the permeability of the capillary bed here and the latter increasing it: this worker's interpretation is open to some doubt, and, in view of the paucity of nerve supply even to the vascular bed, his results may have been obtained by diversion of more blood to other regions following sympathectomy, or vice versa.

These, then, are a few of the problems which confront us. The field is a difficult one, but full of opportunities; the accumulation of data has so far been slow, and it is hoped that the near future will supply the solution to some of the basic problems involved.

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BIRTH WEIGHT AND SUBSEQUENT WEIGHT

BY

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The relation of the weight at birth to subsequent growth of weight and height in children of school age has been shown elsewhere (Illingworth and co-workers, 1949). It was demonstrated that the birth weight has a constant and very important relationship to subsequent weight and a less marked relationship to height at all ages studied (4–13 years). Throughout childhood the average child who was a small baby at birth weighs considerably less than the average child who at birth was a large baby, weighing 8½ lb. (3.85 kg.) or more. Attention was drawn to the absence of reference in the literature to this relationship.

Present Study

This paper is a study of the same relationship in children attending the child welfare clinics in the city of Sheffield. The investigation covers all children born between 1941 and 1945 attending the child welfare clinics whose birth weight we could satisfactorily determine and who fell into the following birth-weight groups:

Group A .. 5 lb. 8 oz. (2.5 kg.) or less.
„ B .. 7 lb. 2 oz. to 7 lb. 6 oz. (3.23–3.35 kg.).
„ C .. 8 lb. 8 oz. to 9 lb. 7 oz. (3.85–4.28 kg.).
„ D .. 9 lb. 8 oz. (4.31 kg.) or more.

There were 276 children in Group A, 275 in Group B, 601 in Group C, and 191 in Group D. The sex distribution was approximately equal. The birth weights of children born on district were obtained from the midwives' antenatal charts, and of those born in hospital from the infant welfare charts. The birth weight on the latter charts is obtained from a note brought by the mother from the hospital to the child welfare clinic. The weights given subsequently are those recorded by the child welfare staff. It is possible that there are certain small errors in these figures, owing, for instance, to inaccuracy of scales, but these errors would apply equally to the four groups studied.

Results

Table I shows the mean weight at various ages of children who belonged to the four birth-weight groups. Some of the records showed the weight at more than one age. All the figures have been utilized for working out the means given. The gaps in the tables are due to an insufficiency of records of the weight of children at certain ages. The maximum error in the age recorded is one month. For example, a child recorded as being 3 years of age would be within one month of his third birthday, but no more. It will be seen that with a very occasional exception, which is explained by the smallness of numbers, there is a constant gradation of weight in relation to weight at birth. The average male child at the age of 1 who weighed 9½ lb. (4.31 kg.) or more at birth (Group D) weighed more (24 lb. 7 oz.—11.08 kg.) than the Group A child at 2 (24 lb. 3 oz.—10.97 kg.), and more at 2 (29 lb. 1 oz.—13.18 kg.) than the Group A child at 2 (28 lb. 9 oz.—12.96 kg.). The average female child in Group D weighed more at 2 (29 lb. 9 oz.—13.41 kg.) than the Group A child at 3 (28 lb. 1 oz.—12.73 kg.).

It is interesting to note that 19 (37.3%) of the male children in Group A weighed less than 20 lb. (9.07 kg.) at the age of 1 year, compared with two children (1.3%) in Group C and D combined. Of the female children in Group A 43.6% weighed less than 20 lb. at the age of 1 year, while none of the 23 female children in Group D weighed less than 20 lb. at that age.

Table II shows the range of variation in these children The table is divided into two parts. The first part concerns children at the age of 1, 1 year 3 months, 1 year 6 months, and 1 year 9 months : the second part concerns children at the age of 2, 2 years 3 months, 2 years 6 months, 2 years 9 months, and 3 years. Where a child attended the clinic more than once, and his weight was therefore recorded at more than one age, only the first of his weight records was used for the table. The " normal " weights used were those given by Paterson (1947). The figures were worked out separately for the two sexes and combined for the purpose of the table. They are shown graphically in the Chart. It will be seen that in the age group 1 to 1 year 9 months 34 (16.8%) of 202 children in Group A were 10% or more below the average weight, as compared with 2 (0.4%) of 526 children in Groups C and D. In Group A 24 (11.9%) children were 10% or more above the average weight, as compared with 199 (50.6%) in Group C and 91 (68.4%) in Group D. Put in another way, of the 46 children in the four birth-weight groups studied who were 10% or more below the average weight 73.9% were children from Group A, and only 4.4% from Group C and D combined. Yet the children in Group A constituted only 22% of the total number.

TABLE I.—*Relation of Birth Weight to Subsequent Weight. Mean Weight at Various Ages. (The figures in parentheses indicate the number of children in each group)*

	Group A	Group B	Group C	Group D
Boys				
Birth ..	lb. oz. 4 14 [2·21 kg.]	lb. oz. 7 4 [3·29 kg.]	lb. oz. 8 13 [4 kg.]	lb. oz. 9 15 [4·51 kg.]
1 year ..	20 12 (51) [9·41 kg.]	22 5 (36) [10·12 kg.]	24 3 (104) [10·97 kg.]	24 7 (44) [11·08 kg.]
1½ years	22 6 (18) [10·15 kg.]	26 2 (23) [11·85 kg.]	25 15 (46) [11·76 kg.]	27 2 (22) [12·3 kg.]
2 „	24 3 (26) [10·97 kg.]	26 8 (26) [12·02 kg.]	28 15 (63) [13·12 kg.]	29 1 (22) [13·18 kg.]
2½ „	28 0 (10) [12·7 kg.]	—	30 14 (15) [14 kg.]	30 11 (10) [13·92 kg.]
3 „	28 9 (10) [12·96 kg.]	—	33 10 (18)* [15·25 kg.]	
Girls				
Birth ..	5 0 [2·27 kg.]	7 4 [3·29 kg.]	8 13 [4 kg.]	9 14 [4·48 kg.]
1 year ..	19 11 (59) [8·93 kg.]	21 13 (48) [9·89 kg.]	22 8 (73) [10·21 kg.]	23 3 (23) [10·52 kg.]
1½ years	21 15 (23) [9·95 kg.]	24 13 (15) [11·25 kg.]	24 10 (31) [11·17 kg.]	25 4 (9) [11·45 kg.]
2 „	24 12 (31) [11·23 kg.]	27 0 (28) [12·25 kg.]	26 15 (64) [12·22 kg.]	29 9 (19) [13·41 kg.]
3 „	28 1 (15) [12·73 kg.]	—	32 8 (20)* [14·74 kg.]	

* Groups C and D are combined owing to smallness of numbers.

TABLE II.—*Range of Variation of Weight at the Ages of 1–3 in Relation to the Birth Weight*

Group	No. of Children	Percentage				
		20% or More Above the Average Weight	10% or More Above the Average Weight	Less than 10% Above or Below the Average Weight	10% or More Below the Average Weight	20% or More Below the Average Weight
Age 1 to 1 ¾ years						
A	202	4	7·9	71·3	14·4	2·5
B	189	13·7	19·6	61·4	4·2	1·1
C	393	23·7	26·9	48·8	0·5	0
D	133	36·8	31·6	31·6	0	0
Age 2 to 3 years						
A	118	1·7	2·5	72·1	12·7	11·0
B	110	3·6	1·8	90	3·6	0·9
C	200	4	17	75·5	3	0·5
D	72	6·9	16·7	75	1·4	0

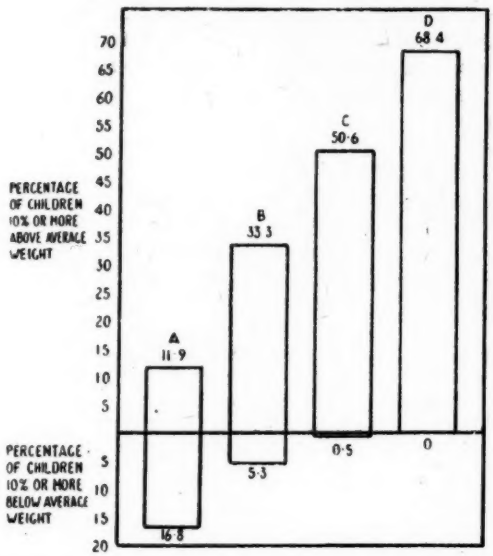

Chart showing relation of birth weight to weight at 1 year to 1 year 9 months.

In contrast, of the 377 children in the groups studied who were 10% or more above the average weight 6.3% were of Group A (in which the total number of children was 202) and 76.9% of Groups C and D (total number of children 526).

Similar differences were found in older children, aged 2 to 3 years. In this age group, for instance, 23.7% of the 118 children in Group A were 10% or more below the average weight, as compared with 1.4% in Group D. In Group A 4.2% were correspondingly overweight, as compared with 23.6% in Group D. Put in another way, of the 70 children in the birth-weight groups studied who were 10% or more above the average weight 7.1% were children from Group A (in which there were 118 children) and 84.3% from Groups C and D (total number of children 272).

Discussion

The investigation shows the great importance of taking the birth weight into account in the assessment of the physical growth of a child. Though some babies who are born prematurely do catch up to the "normal" and sometimes weigh more than the normal for the age, the average weight of a child born prematurely is considerably less than that of a child who was above the average birth weight. That these differences persist throughout childhood has already been shown (Illingworth and co-workers, 1949). The fact that a child is said to be "under weight" is very often a source of great worry to the mother. When due allowance is made for the birth weight it will be found that a considerable number of those so-called under-weight children are of average weight for children of that age, sex, and birth weight.

Summary

The growth in weight up to the age of 3 years of 1,343 children of different birth weights was investigated.

The average male child who at birth weighed 5½ lb. (2.5 kg.) or less weighed consistently less than the average child of a larger birth weight. At the age of 1 the mean weight of the child who at birth weighed 5½ lb. or less was 20 lb. 12 oz. (9.41 kg.) (male) and 19 lb. 11 oz. (8.93 kg.) (female). The mean weight of the child who weighed 7 lb. 2 oz. to 7 lb. 6 oz. (3.23 to 3.35 kg.) at birth was 22 lb. 5 oz. (10.12 kg.) (male) and 21 lb. 13 oz. (9.89 kg.) (female). The corresponding figures for the child who weighed 9½ lb. (4.31 kg.) or more at birth were 24 lb. 7 oz. (11.08 kg.) (male) and 23 lb. 3 oz. (10.52 kg.) (female). The same gradation of weight in relation to birth weight was shown in all the age groups studied.

The average male child who at birth weighed 9½ lb. or more weighed more at 1 year than the child whose birth weight was 5½ lb. or less at 2 years. The average male or female child who weighed 9½ lb. or more at birth weighed more at 2 than the child whose birth weight was 5½ lb. or less did at 3 years.

Mothers are occasioned a great deal of worry by being told that their child is under weight for its age. A considerable proportion of so-called under-weight children are found to be of average weight when due attention is paid to age, sex, and weight at birth.

My thanks are due to Dr. A. Black, principal maternity and child-welfare officer, City of Sheffield, for her great help and co-operation in making her records available for study; to Dr. Gin for her painstaking study of the records; and to the medical officer of health for Sheffield, Dr. Llewellyn Roberts, for permission to publish the results.

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COMPARISON AND ESTIMATE OF GROUP AND INDIVIDUAL METHODS OF TREATMENT

BY

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The Belmont Hospital practice of allotting cases on admission by a rota system enabled us separately to treat similar clinical material between August, 1946, and December, 1948. It seems a reasonable assumption that the rota system ensures a high degree of similarity in the material allocated. Since group therapy was used by one of us (A.S.T.) and an individual approach by the other (N.C.) we considered a comparison of the results of treatment would prove instructive.

In establishing a diagnosis we took the presenting feature—for instance, anxiety, hysteria, or depression—and applied that as the label for our purpose. Although it was recognized that patients often presented more than one of these syndromes, it was thought that this procedure would facilitate appraisal of the results. The term "schizophrenia" includes paranoid states; mental defect has been used as a diagnosis only when it constituted the most important aspect of the case. The organic cases included epilepsy, post-encephalitis, secondary dementia, toxic confusional state, causalgia, carcinoma of the stomach, and severe head injury. Both physical and psychological methods of treatment are compared.

The clinical results have been assessed by means of a questionary sent three months after the patient left hospital. We are indebted to Dr. Louis Minski, who is conducting a follow-up of Belmont patients, for use of the replies. The questionary is as follows:

1. Has your general health been good since leaving hospital?

2. What symptoms, if any, still persist?

3. Have you had further treatment since leaving? If so, state whether from your own doctor or as an out-patient or in-patient of any hospital.

4a. Are you in regular work? b. If not, is this due to your health?

For the purpose of estimating the results we expressed the replies as "yes" or "no," and have interpreted "yes" to both questions 1 and 4a as being a favourable result.

Regardless of the answers to 2 and 3, a "no" in reply to either question 1 or 4a implied an unfavourable result. In other words, a general improvement in health in conjunction with capacity to work regularly is considered a satisfactory finding. It could be argued that this method of interpretation does not allow for the occurrence of a healthy man's being out of work: this did not happen in our experience.

The relative proportions of psychiatric states and the findings of the follow-up in our two series are shown in Tables I and II. With the exception of anxiety states and hysteria the similarity of the figures suggests that we have used the same criteria in arriving at a diagnosis. All cases considered in the comparison are male.

TABLE I.—*A.S.T.'s Cases (Group Therapy)*

Diagnosis	Favourable Result	Unfavourable Result	Not Followed-up	No Reply	Total
Anxiety states ..	28	29	5	9	71 (39·01%)
Hysteria	8	6	1	4	19 (10·44%)
Depression ..	17	6	3	1	27 (14·84%)
Psychopathic personality ..	7	10	1	6	24 (13·18%)
Schizophrenia ..	4	9	2	7	22 (12·09%)
Obsessional neurosis	3	1	2	—	6 (3·30%)
Mental defect ..	—	2	1	—	3 (1·65%)
Organic disease ..	2	7	1	—	10 (5·49%)
	69	70	16	27	182 (100%)

TABLE II.—*N.C.'s Cases (Individual Therapy)*

Diagnosis	Favourable Result	Unfavourable Result	Not Followed-up	No Reply	Total
Anxiety states ..	12	12	3	3	30 (27·52%)
Hysteria	8	8	3	2	21 (19·27%)
Depression ..	11	3	1	2	17 (15·60%)
Psychopathic personality ..	2	3	6	2	13 (11·92%)
Schizophrenia ..	3	5	1	6	15 (13·76%)
Obsessional neurosis	1	—	1	—	2 (1·84%)
Mental defect ..	2	1	—	1	4 (3·67%)
Organic disease ..	—	6	—	1	7 (6·42%)
	39	38	15	17	109 (100%)
Combined totals .. (Tables I and II)	108 37·11%	108 37·11%	31 10·65%	44 15·13%	291 100%

Taking twice the standard error of the difference (Bradford Hill, 1949— $\sqrt{\frac{p_1 \times q_1}{n_1} + \frac{p_2 \times q_2}{n_2}}$) as the test of significance, the observed differences are at the limits of probability. Anxiety states differed by 11.49% (twice the standard error = 11.21) and hysteria by 8.83% (twice the standard error = 8.81). This suggests that anxiety/hysteria represents the two ends of a scale on which there was considerable subjectivity in choice of one or other term.

Forms were not sent to 31 cases (10.6%) of the 291 patients under consideration either because they were Service patients or because it was considered administratively inexpedient. A total of 216 (74.22%) replied, and the average length of time from leaving hospital to their last replies was 10.77 ± 7.01 months (arithmetical mean and standard deviation). In 88 cases (30.24%) more than one reply was received, and the average length of time before their final reply was 13.71 ± 6.34 months. Of these, 76 remained consistently favourable or unfavourable. Of the 108 men who replied favourably 36 were symptom-free and not in receipt of further treatment; 15 had been diagnosed as depressives, nine as anxiety states, and five as hysterics. This finding supports the well-known clinical observation that depression, both quantitatively and qualitatively, yields the best results. The patients who did not reply to the questionary were of interest: we found an undue proportion of psychopathic personalities and schizophrenics—21 out of 44—and suggest they tend to be a prognostically unfavourable group. Considered separately, our results are similar and correspond to those given above for the total group.

Against this background we have tried to compare the use of group and individual therapy. Neither of us invariably used a specific psychiatric treatment for a particular clinical syndrome—for example, not all patients treated by electric convulsion therapy were depressives and not all depressives received E.C.T. It was therefore thought reasonable to give analyses of treatment (Tables III and IV).

TABLE III.—*Treatment of A.S.T.'s Cases*

Type of Treatment	Favourable Results	Unfavourable Results	Not Investigated	No Reply	Total
In hospital 20 days or less	5	10	4	8	27 (14·84%)
Group therapy ..	29	22	6	5	62 (34·08%)
Group therapy and modified insulin	20	13	2	5	40 (21·98%)
Modified insulin ..	4	8	1	3	16 (8·79%)
Electric convulsion therapy ..	5	6	—	—	11 (6·04%)
Insulin comas ..	4	3	—	4	11 (6·04%)
Deep narcosis ..	—	2	—	1	3 (1·64%)
Routine procedure	2	6	3	1	12 (6·59%)
Total ..	69	70	16	27	182 (100%)

Average duration of stay in hospital, 83·9 ± 63·3 days.

TABLE IV.—*Treatment of N.C.'s Cases*

Type of Treatment	Favourable Results	Unfavourable Results	Not Investigated	No Reply	Total	Difference in Percentages (Tables III and IV)]
In hospital 20 days or less	3	2	2	2	9 (8·26%)	6·58
Individual therapy ..	10	6	2	1	19 (17·44%)	16·64
Individual therapy with modified insulin ..	6	6	—	1	13 (11·92%)	10·06
Modified insulin	2	1	1	2	6 (5·5%)	3·29
Electric convulsion therapy	10	2	1	1	14 (12·84%)	6·80
Insulin comas	3	3	1	3	10 (9·17%)	3·13
Deep narcosis	1	4	—	—	5 (4·59%)	2·95
Leucotomy	—	—	1	—	1 (0·92%)	0·92
Routine procedure ..	4	14	7	7	32 (29·36%)	22·77
Total	39	38	15	17	109(100%)	

Average duration of stay in hospital, 100·15 ± 73·95 days.

It was not thought that results could be attributed to in-patient treatment of a few days' duration, so an arbitrary minimum of 21 days has been chosen in compiling the above tables. The tables suggest a much greater subjectivity in choice of treatment than in establishing a diagnosis. Modified insulin is of the type described by Sargant and Craske (1941), and the chief indication for its use was loss of weight. A significantly greater number of patients in Table III were treated in this way than in Table IV: observed difference 13.35% (twice the standard error = 9.98). So far as we can see, it has had no effect upon the results. Taking the specific physical treatments (E.C.T., insulin comas, deep narcosis, and leucotomy) as a whole, the observed difference shown by the tables was 13.8% (twice the standard error = 9.96). N.C. used E.C.T. in depression and deep insulin comas in schizophrenia to a much greater extent than A.S.T.—particularly the former. The chief differences lie in the proportion of patients treated by group and individual therapy (without or with modified insulin) compared with that subjected to routine procedure. The corresponding figures, 16.64%, 10.06%, and 22.77%, are all significant: the respective standard errors are 10.11, 8.73, and 9.47.

Patients treated by group and individual therapy occupied separate wards, and their contacts were of only a

superficial kind. They were subjected to the same routine and had access to the occupational, recreational, and educational facilities offered by the hospital. In addition to seeing medical or surgical specialists they had the opportunity of interviewing a psychiatric social worker and the disablement resettlement officer. The expression "routine procedure" implies the above measures, but indicates that no specific psychiatric technique was used.

The group was an "open" one—that is, new patients were joining as old ones left the hospital. It met for an hour each day and varied in size from eight to twelve members. Originally reference was made to Thomas's (1943) review of the literature, and treatment began with the repressive-inspirational type of therapy. Such books as *Straight and Crooked Thinking* by Thouless (1930), *The Common Neuroses* by Ross (1923), and *How the Mind Works* by Burt and others (1945) were used as a basis for discussion. Lectures were given by the psychologist, the social worker, the disablement resettlement officer, the occupational therapist, and the physical training instructor. Debates on the value of physical training and occupational therapy led to an increased attendance at these activities.

Personalities comprising the group markedly influenced the subject-matter, and papers were read on a wide range of subjects—for example, architecture, radio propaganda, film art, aeronautics, radar, and Zionism. Animated conversations took place on the colour bar, emigration, euthanasia, and sterilization. "Twenty questions" was a favourite activity with one particular group. Psychological subjects—inferiority complex, will power, masturbation, interpretation of dreams, and the needs of the well-balanced life—were popular themes. Group psychotherapy itself came in for criticism. Its advantages were thought to be the opportunity for abreaction, the daily contact with the therapist, increased objectivity, broadening of outlook, and stimulation of ideas, which were argued outside the formal group hours. On the other hand, there was an initial difficulty in persuading patients to give confidences to others whom they distrusted or disliked. As time progressed attempts were made to persuade the group to take an active part in deciding its own activities.

During the period under review the therapist increased the emphasis on psychological treatment. In addition, he has tended, not always successfully, to be more selective in choosing members and to keep the numbers small. Both drug abreaction with intravenous sodium amytal and inhaled ether with a free-association technique have been used—the material provided forming the subject-matter for group discussions. Fenichel's (1946) *Psychoanalytical Theory of Neurosis* was used as a guide at this stage of the group's development. During the two years there has been a shift from an educational to a more strictly therapeutic approach, giving, so far as is practicable, the initiative to the patients themselves.

None of N.C.'s patients had group methods in any form. The psychotherapy given was of a non-analytical and superficial kind. The patients who had this type of treatment were seen on an average twice a week. The basis of the treatment was the establishment of good rapport with the patient—encouraging him to give as complete an anamnesis as possible and using his life story as the basis for reassurance—the expression of painful and unacceptable emotion, and the discussion of unadmitted fears, conflicts, and worries.

As with anxiety/hysteria, so "psychotherapy/routine procedure" comprises another scale along which we have ranged ourselves. A comparative analysis of results is shown in Table V.

TABLE V.—*Analysis of Results*

	A.S.T.'s Cases				N.C.'s Cases			
	Group Therapy		Routine		Individual Therapy		Routine	
	+	−	+	−	+	−	+	−
Anxiety states ..	24	16	—	3	9	6	1	2
Hysteria	7	5	—	—	4	3	2	4
Depression ..	10	2	—	—	1	—	—	1
Psychopathic personality	5	4	1	1	1	1	1	1
Schizophrenia ..	1	3	—	—	—	1	—	—
Obsessional neurosis	1	—	—	—	—	—	—	—
Mental defect ..	—	—	—	1	1	—	—	1
Organic disease ..	1	5	1	1	—	1	—	5
Total ..	49	35	2.	6	16	12	4	14

+ = Favourable result. − = Unfavourable result.

With the physical methods of treatment (E.C.T., insulin comas, and deep narcosis) N.C.'s 14 favourable and 9 unfavourable cases show to advantage against A.S.T.'s 9 favourable and 11 unfavourable cases: this is chiefly due to her treatment of depressives by E.C.T. (Tables III and IV). In Table V the figures for psychotherapy/routine procedure give the opposite result owing to the inclusion of depressives in the group-treated material. It will be noticed that both our figures for psychotherapy are better than those for routine procedure, and that we fared slightly better with those having anxiety states than cases of hysteria. Excluding the depressives there is no difference between the results of group and individual treatment.

A small number of group and individually treated cases had E.C.T., insulin comas, or deep narcosis. They have been included under the heading of the appropriate physical method, but are too few to provoke comment. The greater proportion of patients receiving group treatment is due to the nature of the group. Attendance ranged from a casual appearance at an educational or diversional class to a conscious attempt at treatment. Of course, one merges into the other, and it seems that in turning the group into a debating society or a playground was itself a therapeutic process for a few patients. The best results have apparently been achieved by discussion of personal problems and case histories (see Table VI).

TABLE VI.—*Results of Group Therapy*

	Discussion of Personal History		Educational or Recreational		Casual		Total
	+	−	+	−	+	−	
Anxiety states ..	10	2	9	7	5	7	40
Hysteria	1	—	4	3	2	2	12
Depression	2	—	5	1	3	1	12
Psychopathic personality	2	2	3	2	—	—	9
Schizophrenia ..	1	1	—	1	—	1	4
Obsessional neurosis	1	—	—	—	—	—	1
Organic disease ..	—	—	—	3	1	2	6
	17	5	21	17	11	13	84

+ = Favourable result. − = Unfavourable result.

The inclusion of organic disease—epilepsy, post-encephalitis, or secondary dementia—may require explanation. These patients, although told the procedure could have no therapeutic value, insisted on attendance, and while they were in hospital it seemed to lessen their sense of isolation. The same consideration also applies to the poorer psychiatric material. Patients with anxiety states and hysteria derived most benefit from group therapy and those with anxiety states in particular derived benefit from the discussion of personal case histories.

In addition to the effects of therapy the influence of age, length of illness, intelligence, and the presence of

associated physical disease has been considered in our joint group of patients with anxiety states and hysteria. An analysis of these factors in our material is given in Table VII.

TABLE VII

	Favourable Results	Unfavourable Results	Observed Difference Two Previous Groups	Twice Standard Error
Average age ..	30·14 ± 7·82	38·45±11·53	8·31	3·74
Average length of illness	3·43 ± 4·61	6·05±7·48	2·62	2·30
Incidence associated physical disease.. ..	14·29%	34·54%	20·25%	15·88
Incidence Selection Groups 1 and 2	30·61% } 49 cases	16·07% } 44 cases	14·54%	17·20
Incidence Selection Groups 4 and 5	10·21% }	34·09% }	23·88%	16·68

Increasing age, length of illness, and associated physical disease—for example, bronchitis, rheumatism, duodenal ulcer, asthma, and colitis—were adverse factors in our experience. Intelligence below the average (Selection Groups 4 and 5) occurred significantly in the unfavourable replies. Although superior intelligence (Selection Groups 1 and 2) is seen more often in the favourable results, this did not happen to a significant extent. Intelligence has been assessed by Dr. Desai, using the matrix test, and graded in terms of "selection groups"—the average being taken as S.G. 3+ and 3−. That older and less intelligent patients do not respond to psychotherapy is a well-known clinical observation.

There are other constitutional factors which may have affected the results, but we did not study them adequately. The neurotic constitution described by Slater (1943) is clearly of the greatest importance. Unstable personalities are often unable to take an interest or co-operate in therapeutic attempts. We would suggest that an active interest in group or individual therapy is itself a favourable prognostic sign.

Summary and Conclusions

Similar clinical material has been separately treated by two methods—in groups (69 cases) by A.S.T., and individually (38 cases) by N.C.—the results of which are compared.

The incidence of psychiatric syndromes corresponds closely in the two groups, with the exception of anxiety states and hysteria, the proportions of which are significantly different. It is argued that this difference is partly due to a subjective emphasis upon one or other term.

The results of treatment, as judged by means of a questionary, were found to be similar for both groups.

Comparing and analysing treatments, we found significant differences in the use of physical and of psychotherapeutic methods by both therapists. Such differences were due to personal preference.

Comparing the use of physical treatment, A.S.T. was found to use more modified insulin, but obtained no better results. E.C.T., insulin coma, and deep narcosis were preferred by N.C., who obtained better results from them, this being due to a greater use of E.C.T. in depression.

The difference in psychotherapy lies in the exclusive use of either group or individual methods. The results of treatment by either technique are the same. A.S.T.'s rather better figures are attributable to his preference for group therapy in depression. Psychotherapy of either type yields better results than routine treatment. Within the group, discussion of personal case histories produces better results than educational methods, but the numbers are too small for final conclusions to be drawn.

Apart from treatment, such constitutional factors as age, low intelligence, length of illness, and the presence of associated physical illness significantly affect prognosis. It is tempting to suggest that interest in either group or individual therapy is itself a good prognostic sign.

Our thanks are due to Dr. Louis Minski not only for permission to publish this paper but for freedom of choice in methods of treatment. We are also indebted to Dr. Desai for helpful criticism in writing the paper.

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PRIMARY TORSION OF THE OMENTUM IN CHILDREN

BY

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Torsion of the great omentum in its long axis is recognized in the adult as a cause of acute abdominal symptoms, and there are numerous references to it in the literature (Draper and Johnson, 1931; Lipsett, 1941). In the child the omentum is poorly developed and is usually short, filmy, and relatively free from fat; therefore, from its nature, any twist will return immediately to normal For this reason torsion of the omentum is rare in childhood

Two types of torsion are recognized: primary or unipolar, where no obvious cause can be found within the abdominal cavity; and secondary or bipolar, where some additional point of attachment is present, such as a focus of inflammation, a hernial sac, or the adhesions of a previous laparotomy. Three cases of primary omental torsion causing acute abdominal symptoms are reported.

Case 1

A previously healthy girl aged 6 was admitted to hospital on October 27, 1947, with the complaint of sudden abdominal pain. This began in the lower abdomen 24 hours before admission and was followed by vomiting on two occasions. About eight hours after the onset the pain settled in the right side of the abdomen and remained there. The appetite was not particularly affected; the bowels had moved four hours before admission. There were no other relevant points in the history.

On examination she was seen to be robust though not obese: the tongue was clean and there was no pyrexia; the pulse was quickened, but the respiratory rate was within normal limits. The whole of the right side of the abdomen was tender to palpation and there was muscle-guarding in the right hypochondrium and to a less degree in the right iliac fossa. Rectal examination was inconclusive. No abnormality was detected in the heart, lungs, or urine. A diagnosis of acute appendicitis was made, and laparotomy was carried out through a grid-iron incision in the right iliac fossa.

At operation some clear free fluid was found in the peritoneal cavity. The caecum, appendix, and small bowel showed some superficial injection. Exploration of the upper abdomen with a finger disclosed a mass in the region of the gall-bladder. It was freely mobile and was delivered without difficulty into the wound. It was then obvious that this was an omental torsion involving most of the greater omentum, and it was ligated at its pedicle and removed. Appendicectomy was then performed and the abdomen closed. Convalescence was uneventful apart from a temporary collapse of the right upper lobe following the anaesthetic.

Pathology.—The specimen was pyriform in shape and measured 7 by 5 cm. It was firm in consistency and plum-coloured, and at the neck the normal omentum was present.

appearing to have undergone two complete turns. On microscopical section some lymphocytic infiltration was found, with haemorrhagic infarction and thrombosis of the vessels. There was no evidence of any active inflammation or tumour formation.

Case 2

A girl aged 4 was admitted to hospital on September 10, 1948, with a history of abdominal pain of five days' duration. The pain had been intermittent and mainly right-sided, and became more severe 18 hours before admission. There was no vomiting and the bowels were opened the day before admission.

On examination the child was flushed; her temperature was 100° F. (37.8° C.), pulse 125, and respirations 20. A small mass was palpable above the inguinal ligament on the right side and there was some muscle-guarding. Rectal examination confirmed the presence of this mass, and an appendix abscess was thought to be present.

At operation the omentum was found to be lightly adherent to the anterior abdominal wall below and to the right of the umbilicus, and in its right half had undergone a torsion. The twisted omentum was removed and appendicectomy performed. The pathological appearances were similar to those in Case 1, the only difference being in the size of the specimen, which measured 3 by 1.5 cm.

Photograph of specimen in Case 3, showing the intense congestion present and the twist at the junction of the free omentum and the infarcted portion.

Case 3

A female child of 4 years was admitted on June 6, 1949, with a history of colicky abdominal pain of six months' duration. The present attack was of 24 hours' duration, and was similar in onset to that in Case 1. Once again the pre-operative diagnosis of acute appendicitis was made and at operation the appendix was found to be normal, but the exploring finger discovered a freely movable mass in the right hypochondrium. This was delivered with ease, and proved to be a twisted omentum. It was ligated at its pedicle and removed. Appendicectomy was also carried out.

The specimen (see accompanying illustration) measured 4 by 4 cm., was quadrilateral in shape, darkly plum-coloured, and almost necrotic in places.

Discussion

Erdmann (1921) reports a case of omental torsion associated with an acute appendicitis in a boy aged 14. At operation a dark necrotic mass was found high up; this proved to be the right half of the omentum, which had twisted on itself three times. The appendix may well have been the initiating factor in this case, which seems to have been a secondary torsion.

Apart from a report by Barsky and Schwartz (1937) in a child of 5, I have found no reference to this condition in children. In the case reported by them repeated attacks of abdominal pain were attributed to a fibrotic omentum which was found at operation.

Torsion without cause is a rare condition. Among various exciting factors that have been suggested as causes of the twist are irregular peristalsis of the bowel due to various causes, from over-violent cathartics to abdominal trauma and irregular fat deposits in the omentum. Payr's theory of haemodynamic torsion is a somewhat fanciful idea, and is without proof. Venous congestion is said to cause the relatively more tortuous veins to twist round the arteries and initiate the torsion. The omentum normally undergoes a purposeless movement within the abdominal cavity. This motility is utilized should any inflammatory process be present within the abdomen when an attempt is made to localize the pathogenic organisms or wall off any necrotic tissue present. It is difficult to understand why this movement should result in an acute twist which is maintained and which is sufficient to cause necrosis of the omentum itself.

A pre-operative diagnosis is unlikely in this condition, laparotomy being undertaken for what appears to be an appendicular inflammation. It is also conceivable that even at operation an accurate diagnosis may not be made when laparotomy is carried out through a small incision in the right iliac fossa. On opening the peritoneal cavity free fluid and enlarged glands may be found and the upper abdomen be inadequately explored, the symptoms of the acute abdomen being attributed to lymphadenopathy, which is often found. Left within the abdomen, the twisted omentum will ultimately resolve and become fibrosed, though abscess formation has been described in the adult from what was believed to have been an acute torsion. The treatment advocated, therefore, is excision of the twisted omentum.

Summary

Three cases of omental torsion are reported as a cause of acute abdominal symptoms in childhood.

The rarity of the condition in children is presumably due to the poorly developed omentum in the small child.

The aetiology of the condition is not known, and the diagnosis is unlikely before laparotomy.

Treatment is simple, and consists of resection.

I wish to thank Mr. Matthew White for his help in the preparation of this paper and for his permission to report Cases 2 and 3, which were treated in his wards at the Royal Hospital for Sick Children, Glasgow.

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Recommendations for modernizing measures against the international spread of yellow fever along the routes of human travel have been made by a panel of experts headed by Dr. A. F. Mahaffy, formerly Director of the Yellow Fever Research Institute at Entebbe, East Africa, meeting recently at Geneva under the auspices of the World Health Organization. These recommendations are being considered by the WHO Expert Committee on International Epidemiology and Quarantine meeting in Geneva, which is drafting new international sanitary regulations to replace the present out-of-date conventions. The panel agreed that, while eradication of *Aëdes aegypti* is now practicable, the eradication of yellow fever is still remote because of the presence of the infection in wild monkeys from which the disease may be transmitted by forest mosquitoes to human beings. Although no great urban epidemics have been registered since 1928 in Rio de Janeiro for the Americas, and since 1937 in Dakar for Africa, the panel insisted that outbreaks are still a possibility should the virus be introduced into areas infested by *A. aegypti*. It recommended that adequate precautionary measures should be taken by individual countries, and considered the eradication of *A. aegypti* to be of major importance.

THE STOMACH OF THE RECENTLY DECEASED*

BY

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A vast literature exists on the subject of gastric pathology, but we are still ignorant of the true incidence and severity of "simple chronic gastritis" among the general population. Figures relating to the presence of such gastritis in resected stomachs have a value limited by the presence of peptic ulceration or neoplasm. Opportunities for gastric biopsy are few; moreover, a piece of gastric mucosa removed at biopsy is insufficiently representative of the whole mucosa. Again, a patient's symptoms are an unreliable indication of gastritis.

Gastritis is not merely an interesting academic problem. It is a popular and widely accepted opinion that chronic gastritis is a common condition, but the truth is that in clinical practice, in the majority of cases, we do not know whether it is the man or his stomach that is at fault. Meanwhile vast quantities of stomach sedative will continue to be prescribed at no mean cost to the State.

Valuable information concerning the condition of the stomach can be obtained if the organ is adequately fixed immediately after death. Early fixation is essential for accurate interpretation of the morbid-anatomical findings. Magnus (1937a, 1937b) re-stressed the necessity for this. He showed that autolysis begins usually within 30 to 45 minutes of death in the adult, though much later in the foetal stomach, and that fixation by intraperitoneal injection, as first practised by Faber 50 years ago, is inadequate, whereas direct intragastric injection of fixative soon after death gives excellent results. The technique of intragastric fixation requires the minimum of skill and apparatus, yet it is a method which has been remarkably neglected. Many have regarded the procedure as a ghoulish business. To become sentimental in this way is to impede good and useful knowledge. The manipulation of the corpse is naturally unpleasant but in no way irreverent.

Magnus examined over 30 stomachs fixed shortly after death in patients whose principal disease was not gastric. This series, to my knowledge, represents the largest recorded. My own series includes 62 unselected post-natal stomachs, the majority of which were adult, and 10 foetal stomachs. They were all formalin-fixed according to Magnus's rulings.

Technical Procedures

Fixation.—All the stomachs were fixed with 10% formol-saline. Adult stomachs were fixed within one-half to three-quarters of an hour of death. An ordinary oesophageal tube, permanently strengthened with a length of strong pliable wire, was passed over the tongue and along the posterior pharyngeal wall into the stomach. Then 1½ to 2 pints (0.85 to 1.14 litres) of fixative was quickly poured down the tube through a large glass funnel. Alternatively, fixation can be effected by passing a large-bore needle into the stomach through the seventh or eighth left intercostal space or through the epigastrium. This method, however, is uncertain in its results. Children's and infants' stomachs require an appropriately smaller amount of fixative, passed into the stomach through either a No. 4 Jaques stomach-tube or a wide-bore needle. The stomachs of large foetuses were filled by direct intubation or by needling. Those of smaller foetuses were removed from the abdomen and immersed in fixative.

Macroscopic Examination.—At necropsy the oesophagus, stomach, and duodenum were removed as one piece. Each stomach was opened by an incision in the anterior wall midway between the curvatures. After careful examination of the mucosa the specimen was then immersed in formol-saline for at least 24 hours. Later, representative pieces of stomach wall were taken from at least five sites: (*a*) oesophago-gastric junction, (*b*) fundus, (*c*) body, (*d*) pyloric antrum, and (*e*) pyloro-duodenal junction. These were kept in formol-saline for a day or two, then washed, dehydrated, embedded in paraffin, and stained with haematoxylin and eosin. Special stains, such as those for mucin, Paneth's cells, argentaffine cells, collagen, and fibrin, while giving a pleasant picture, were not considered essential.

Morbid-anatomical Findings

As the result of a careful macroscopic and microscopical examination, each stomach, considered as a whole, was placed in one of five grades: Grade 1, normal; Grade 2, showing mild chronic gastritis; Grade 3, showing rather more severe chronic gastritis; Grade 4, showing severe chronic gastritis; Grade 5, showing very severe chronic gastritis. Only stomachs in Grades 4 and 5 could be considered to have "serious" gastritis. No case of pure acute gastritis was encountered, although many of the cases of chronic gastritis showed a greater or less acute inflammatory element.

Before recording the results of investigation it is necessary to consider the normal mucosal structure and also what is understood by chronic gastritis

Normal Gastric Mucosa.—Histologists are more or less agreed upon the glandular structure of the mucosa, but there is still some confusion concerning the cellular elements of the mucosal stroma. The stroma of the healthy adult stomach contains reticulum cells, lymphocytes, plasma cells, and scanty polymorphs. No plasma cells were ever found in the foetal or early post-natal stomachs. They are fairly abundant in later life, even in the healthy mucosa. Probably they arise from the reticulum cells (Lowenhaupt, 1945; Bessis and Scebat, 1946; Fagraeus, 1948), and it is possible that they serve a useful physiological purpose.

Chronic Gastritis.—There is a current belief that the presence of more than a few plasma cells and lymphocytes in the stomach mucosa spells chronic gastritis. This is an erroneous view. In the intestine the normal mucosa contains abundant plasma cells and lymphocytes, yet many would deny the stomach this privilege. As already mentioned, they probably serve a useful physiological function. Only when there are parenchymal changes accompanied by considerable inflammatory cell infiltration is one entitled to diagnose gastritis histologically. "Intestinalization" of the gastric mucosa—i.e., the appearance of goblet cells and Paneth's cells—is characteristic of the severe grades of chronic gastritis. A mucosa very severely affected by chronic gastritis shows great devastation, with considerable degeneration, atrophy, and disappearance of glands, and frequently enormous stuffing of the stroma with chronic inflammatory cells.

No case of diffuse non-inflammatory atrophy of the gastric mucosa, corresponding to Lubarsch's diffuse atrophic pangastritis, was found. A characteristic of

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chronic gastritis is its patchy nature. Although the antro-pyloric part of the stomach was commonly diseased there was no obvious predilection for this region. The severity of inflammatory lesions in the immediate vicinity of ulcers as contrasted with the mildness of such lesions in the mucosa a little more distant was often observed, suggesting that the inflammation was secondary to the ulcer, and not vice versa.

The severity of histological lesions tends to increase with age (see Table). By applying the χ^2 statistical test

Table Showing Number and Age of Stomachs in Each Grade (72 Cases)

Grade	Age of Stomach in Years										Total
	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	81–90	91+	
1	14*	1		1	1			2			19
2	4			1	1		3	3	2		14
3	1		2	1	3	5	5	2		2	21
4				1		6	1	8	1		17
5								1			1

* Including 10 foetal.

(the "exact χ^2 method") it can be demonstrated that the odds are 100 to 1 that histological grading does depend on age. Eliminating foetal stomachs, the odds are about 50 to 1. But 5 out of 16 stomachs in the 71–80 years group and 2 out of 3 in the 81–90 years group were remarkably healthy.

There is definite proof that with increasing age there is a diminishing power of gastric secretion (Bloomfield and Polland, 1933; Davies and James, 1930–1). After the age of 40 the production of HCl and pepsin by the stomach of both sexes diminishes. Above the age of 60 about 60% have histamine-fast achlorhydria. Ivy in 1942 stated that no unchallengeable evidence existed concerning the effect of senescence on the morphology of the stomach. The present series revealed no obvious cause-and-effect relationship between age *per se* and atrophy *per se*.

Aetiology of Chronic Gastritis

Many agents are said to be capable of producing gastritis:—(1) *Exogenous agents*: mechanical and chemical irritants (2) *Endogenous agents*: (*a*) infections, (*b*) hyperchlorhydria, (*c*) metabolic substances—e.g., in uraemia and in burns, (*d*) avitaminoses—e.g., in sprue, (*e*) venous stasis, and (*f*) possibly nervous stimulation of the stomach.

Attention will be focused on the influence of infections and uraemia. Many observers, from Beaumont (1838) onwards, have bracketed infection with gastritis—e.g., gastritis was noted in association with influenza (Vimtrup, 1929) and with diphtheria (Nyfeldt and Vimtrup, 1932). Experimental gastritis has been produced by the injection of bacterial substances (Enriques and Hallion, 1893; Einar Thomsen, 1925). Many have described gastritis in association with uraemia.

An analysis of the necropsy specimens revealed the following data.

Group 1 Specimens (19 stomachs, including 10 foetal and 5 adult).—Of the five adults four had moderately severe bronchopneumonia. In addition one showed severe urinary infection, one fairly severe intestinal infection, and one marked bronchiectasis and uraemia. Arteriosclerosis of any magnitude was found in only one adult stomach—in one of the cases with moderately severe infection. The four infants whose stomachs were in this group had no infection at necropsy.

Group 2 Specimens (14 stomachs).—There was infection in 10 cases—principally pulmonary in seven, principally urinary in two, wholly peritoneal in one. Uraemia was present in only one case. Arteriosclerosis of any magnitude was found in only two stomachs.

Group 3 Specimens (21 stomachs).—There was infection in 12 cases—principally pulmonary in seven (including two cases of tuberculosis), principally urinary in one, one case was an ulcerating carcinoma of the hepatic flexure with a small paracolic abscess, another a tuberculous spine, and two were cases of acute gastro-enteritis. There were two cases of uraemia, one of which showed infection also. Arteriosclerosis was present in only two stomachs. The cases without infection or uraemia included a case of multilobular cirrhosis of the liver, a case of Hodgkin's disease, and a case of status asthmaticus.

Group 4 Specimens (17 adult stomachs).—Infection was present in eight cases—principally pulmonary in six, principally urinary in two. Uraemia was present in five cases, accompanied by infection in four of these. Arteriosclerosis of moderate severity was present in three stomachs. Two of the cases in this group were of suspected nutritional deficiency.

Group 5 Specimen.—This patient was an adult suffering from hypertension with cerebral changes and a fractured femur. There was no mention of infection in the necropsy report, but this cannot be excluded, and was, in fact, a strong probability.

Thus, infection was established in roughly one-half of the 72 cases, or, excluding the foetal stomachs, in about 60%. Chronic infection was twice as common as acute infection, and of the chronic infections pride of place went to bronchiectasis and pyelonephritis. Infection was not present to a significant degree in all cases of severe gastritis, yet it was sometimes found to be marked in cases with mild gastritis or in association with anatomically normal stomachs. Uraemia was present in nine cases, but six of these also had extragastric infection. It was invariably accompanied by gastritis, often severe.

Ulcers and Erosions

Ten of the cases showed one or more ulcers in the stomach—i.e., 15% of the adult stomachs. Acute ulcers were present in four stomachs and chronic ulcers in seven. The average age of the patients with ulcers was 67. In no instance had ulcer been diagnosed during life. Six of the ulcerated stomachs showed severe gastritis, three showed milder gastritis, and in one carcinoma ventriculi was present.

Hart (1918–19) and Stewart (1929) found chronic peptic ulcers or scars thereof in 10% of all necropsies. Doll (quoted by Avery Jones, 1947) made a statistical survey of working men in industry and transport and found a 5–7% incidence of peptic ulcer. Avery Jones (1947) studied 615 peptic ulcer patients. Of these, two-thirds were males and 33% were over 60. He drew attention to the apparently increasing age of the ulcer population and to the considerable rise in mortality in those patients over 60 who have not had surgical assistance.

A study of the material under review suggests that the increasing incidence of ulcers in the older age groups is related more to failure of the general health of the patient than to local factors. Excluding the case of carcinoma ventriculi, seven out of the nine cases of gastric ulcer were patients with extensive extragastric infection: one patient had pneumonia with purulent pericarditis, another bronchial carcinoma, three had bronchiectasis, and two had severe urinary infection.

Erosions were found in 18 stomachs—i.e., in 30% of post-natal stomachs. In four of these there was also ulceration. These erosions showed no characteristic distribution. They appeared in any part of the mucosa. They varied in size and shape from minute round specks, just visible to the naked eye, to round, oval, or irregular excavations. In depth they varied from simple desquamations to

neo-ulcers. They were frequently multiple. They were or were not accompanied by gastritis. Often they showed evidence of recent or old haemorrhage. The simplest erosions were minute deficiencies in the superficial part of a congested but otherwise normal mucosa. The edges of these erosions had a pale blurred appearance due, presumably, to the digestive action of gastric juice.

Polymorphs were or were not present. Sometimes they formed a distinct cuff around the edges of an erosion. Other erosions were simply miniature ulcers, stuffed with polymorphs and set in a very inflamed mucosa. Most, if not all, of the erosions without polymorphs were agonal, nevertheless the underlying mechanism of production may play an important part in the pathogenesis of some, perhaps many, erosions and ulcers. One may suggest that contractions of the muscle wall of the stomach produce haemorrhages which burst through the covering epithelium. Support is lent to the importance of a vascular origin for these agonal erosions by three facts : (1) their localization to minute areas of mucosa, (2) their frequent occurrence in an otherwise normal mucosa, and (3) the almost invariable finding of whole or altered blood in them.

The gastro-intestinal mucosa is immensely rich in blood vessels, and it is probable that rupture of these vessels is a frequent pre-erosion phenomenon. It is likely, therefore, that many so-called primary peptic secondary haemorrhagic erosions are really primary haemorrhagic secondary peptic.

Summary

The examination of 72 unselected stomachs, formalin-fixed according to Magnus's rulings, is described.

The specimens were divided into five histological grades according to their health or disease.

The need for a stricter standard of histological diagnosis of chronic gastritis is emphasized.

It is shown that the severity of chronic gastritis tends to increase with age.

Uraemia was constantly associated with chronic gastritis, often of severe degree. Severe chronic infections were often, though not invariably, associated with chronic gastritis.

Ulceration of the stomach was found in 15% of adult cases; the average age of these patients was 67. The ulcers were undiagnosed during life.

Erosions were discovered in 30% of the non-foetal stomachs. Many of these were agonal.

It is suggested that a vascular origin for erosions and ulcers is commoner than has been supposed.

I wish to express thanks to the University of Edinburgh for permission to publish this report; to the many members of the staff of the Central Middlesex Hospital who made this work possible, especially Drs. J. D. Allan Gray, Walter Pagel, and Avery Jones for sustained help and encouragement; and to Dr. George Discombe for statistical assistance.

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DIPHTHERIA IMMUNIZATION WITH P.T.A.P. IN ADULTS

BY

Th. M. VOGELSANG, M.D.(Oslo)

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During the last diphtheria epidemic in Bergen, in 1942–5, an extensive immunization campaign against diphtheria was carried out among school-children. This active immunization was probably largely responsible for a gradual but definite shift in the age distribution of the patients. While the frequency of diphtheria showed an appreciable decline among school-children, the disease attacked adults with an increasing frequency, both relative and absolute. Accordingly there is reason to extend the immunization to include susceptible older children and young adults (Vogelsang, 1949).

In such subjects the prophylactic most commonly used—alum-precipitated toxoid (A.P.T.)—may give unpleasant reactions after inoculation. It is therefore recommended to use instead toxoid-antitoxin floccules (T.A.F.) which, however, is a less efficient antigen and is given in three injections, each of 1 ml., at intervals of three or more weeks.

Holt (1947) has produced a purified toxoid, aluminium-phosphate precipitated (P.T.A.P.), which is said in its antigenicity, stability, and freedom from reactions to have distinct advantages over A.P.T. (Holt and Bousfield, 1949) Studies on the immunizing power of this new prophylactic have been carried out in nurses and medical students.

The subjects were first Schick-tested, and only the Schick-positive were immunized with a batch of P.T.A.P. E.3160 R, Lf 10, 10 mg. $AlPO_4$/ml. The doses given were two inoculations, each of 0.5 ml., intramuscularly in the left fossa supraspinata, with an interval of one month between

the inoculations. Just before the first and the second inoculation and one month after the second, the serum antitoxin titres were determined by the intracutaneous rabbit method of Jensen (1933). The results are given in the Table.

The Diphtheria Antitoxin Titres of the Serum of 31 Persons After Intramuscular Inoculations of P.T.A.P. in 0.5-ml. Doses containing Lf 10, 10 mg. $AlPO_4$/ml.

A.U./ml.	Before First Inoculation	Before Second Inoculation	One Month After Second Inoculation
>10		5	8
1–10		9	13
0·1–1		8	7
0·01–0·1	3	6	3
0·001–0·01	12	2	
<0·001	16	1	
	31	31	31

As most of our nurses and medical students had already been immunized against diphtheria during the war, the series is very small, consisting only of 31 non-immunized Schick-positive persons between 20 and 25 years of age. While three of these before the immunization had an antitoxin titre of between 0.1 and 0.01 A.U./ml. the others had less than 0.01 A.U./ml., which is usually considered to be the borderline between Schick-positivity and Schick-negativity—the Schick level.

After the first inoculation there was a good rise in the antitoxin titres, but three of the subjects still had an antitoxin titre below the Schick level. After the second inoculation all had responded to the immunization with a rise in the antitoxin titre above the Schick level. Most of them reacted quickly to the inoculations to give a very high antitoxin content in the blood. There will, however, always be some persons who are poor antitoxin producers—e.g., one of the nurses had the following three titres: 0.001, 0.001, and 0.1 A.U./ml.

There were no severe reactions after the inoculations. A few of the subjects had a transitory tenderness in the inoculated area for one or two days.

Summary

In a small series the response to immunization with P.T.A.P. in Schick-positive adults was determined by the intracutaneous rabbit method of Jensen. Most of the subjects reacted quickly to the inoculations with a very high antitoxin content in the blood. No general or severe reactions occurred. In a few cases there was a trifling local reaction in the inoculation area. In this series there were no Schick-negative allergic persons.

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A plan under which the World Health Organization will establish its headquarters in the Palais des Nations at Geneva under a 99-year lease was tentatively approved by the WHO General Assembly now meeting in New York. The plan provides for certain constructions to be added to the Palais at a cost of 3,684,000 Swiss francs—a saving of 33% as compared with the cost of earlier projects. The building is expected to provide space for 210 additional offices; it represents an economy of from 1 to 2 million Swiss francs on the cost of the original project approved in July by the WHO Executive Building Committee pending a decision of the United Nations' Board. The Building Committee has paid tribute to the generosity of the Swiss Government in its proposals for financing WHO headquarters, and has accepted the Swiss offer of a grant of 3,000,000 Swiss francs.

Medical Memorandum

"Autemphysesis"

Many bizarre clinical pictures are at times produced by the malingerer. The deliberate injection of air into the soft tissues and the consequent formation of surgical emphysema over a wide area of the body is a resource rarely adopted.

Zachary Cope (1948) quotes the following lines from a lecture delivered by Astley Cooper: "A young man who did not like the idea of going as a soldier endeavoured to make himself as it were a patient or sick person with a view to get off by going before a surgeon to examine him and say he was not capable of performing his military office; well, what did he do? He made a very small opening in his scrotum, and then with a long pipe blew air in at the aperture which made a very large tumour indeed and appeared as if he had got an inguinal hernia—he walked nine miles to the surgeon and nine miles back again, but of course the surgeon was too well aware of the case as to be deceived."

I was recently confronted with a patient whose face and neck had suddenly become swollen. The soft tissues of his face were thickened, his features were almost unrecognizable in the gross swelling. His eyes were shut by the tumefaction of his orbit and eyelids. The soft tissues of the neck were also involved and presented the appearance of Ludwig's angina.

Palpation revealed surgical emphysema over the affected area. He was admitted to the ward for observation, and within 48 hours all the air had been absorbed and the structure of the face and neck had returned to normal.

The patient's nose and throat were carefully searched, but no organic lesion could be detected to account for these puzzling signs, until attention was drawn to a minute, partly healed incision on the inner side of the left cheek. On questioning, he confessed that this was a self-inflicted injury. He was a German prisoner of war and had been in captivity for several years. He had been arrested for an infringement of some camp regulations. To evade or delay the ensuing penalties he had decided to feign sickness.

He also stated that this particular device was not uncommon amongst the troops in the German Army. This was confirmed later after conversation with several German medical officers, also prisoners of war.

The inner side of the cheek, as far back as possible, is nicked deeply with a small fragment of a safety-razor blade. Sometimes, instead, the cheek is forcibly nipped between the molar teeth, so as to produce a punctured wound of the mucosa. The nostrils are then pinched together by finger and thumb and the cheeks are forcibly distended with air, as in the act of inflating the Eustachian tubes. Apparently quite a high pressure is required initially to force air through the hole, but, once a track has been formed, the tissues can be rapidly inflated.

The resulting appearance of this self-inflation, for which Dr. Vertue kindly suggested the name of "autemphysesis," is puzzling to those who have not seen it before.

I am indebted to Brigadier Monro, surgical consultant to Middle East Land Forces, for permission to report this case.

PHILIP READING, M.S., F.R.C.S.

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Reviews

CLINICIAN'S GUIDE TO THE VITAMINS

The Vitamins in Medical Practice. By J. Shafar, M.D., M.R.C.P. (Pp. 383. £1 5s.) London: Staples Press. 1949.

The design of the book falls into three parts. In the first a good description is given of the chemical composition, sources, and physiological actions of the vitamins, and of the pathological effects resulting from their deficiency in man and animals. Two useful chapters follow, on the effects of cooking, canning, and fermentation upon the vitamin content of foodstuffs, and on the toxic and pharmacological aspects of the vitamins. The second part of the book—some 35 pages—describes the accepted major clinical syndromes resulting from depletion of one or more of the vitamins. An adequate account is given of beri-beri, pellagra, scurvy, and rickets.

In the third and most interesting section the author discusses the problems of vitamin deficiency in pregnancy, infancy, and childhood. He has in addition collected a large amount of information on the effects of vitamin deficiency on the different systems of the body—e.g., in disorders of the heart, gastro-intestinal tract, endocrine glands, bone marrow, skin, and the oral structures. Specialists in these branches of medicine will be able to obtain a concise review of the literature on their own particular problems without having to hunt through a mass of material on the general aspects of nutritional disease.

In the preface the author states that a primary consideration has been that the subject should be covered as concisely as possible without sacrificing essential material. In this he has been successful, for the reader has been provided in 365 pages with a large mass of information on almost every conceivable aspect of the vitamins in health and disease, carefully selected and documented with no fewer than 1,684 references. As such, the book will be of real value to the physician who already has or wishes to obtain a sound insight into the effects of vitamin deficiency on the individual as a whole and on the various systems which together comprise the individual. The book should also appeal to those reading for higher medical examinations.

To the average general practitioner in Great Britain the book will be too detailed in many respects, while lacking one feature which he will probably feel most essential—a well-balanced discussion of the present position in this country of nutritional deficiency states in general and the vitamin deficiencies in particular. Is he to believe that frank vitamin deficiency diseases are as rare as is so frequently stated, while latent or subclinical deficiency states are as common as some physicians suggest? The general practitioner's principal need is for simple but detailed guidance on the difficult problem of the differential diagnosis between the clinical features of frank and subclinical deficiency diseases and of organic and functional states leading to similar clinical pictures. This, with a detailed description of how to take a dietary history and how to remedy a defective or ill-balanced diet, is of more importance and interest to him than an elaborate account of the chemical composition of the vitamins and the physiological mechanisms by which they achieve their effects.

In short, the book may be classified as an excellent compilation and a well-balanced review of the literature on vitamins rather than a contribution of original work or ideas to this important subject.

L. S. P. DAVIDSON.

CARCINOMA OF THE CERVIX

Cancer of the Uterine Cervix. By F. Truelsen. (Pp. 440. No price.) Copenhagen: Rosenkilde and Bagger. London: H. K. Lewis.

This is the English translation of Frithiof Truelsen's book, which has for its main purpose the publication of the results obtained in Copenhagen by treating carcinoma of the cervix with radiotherapy. The cases number 2,918, and the results are illustrated by the following sample figures: between 1934 and 1937, 881 cases were seen; an absolute cure rate of 34.6% and a relative cure rate of 38.7% were obtained.

The book contains far more than figures and statistics. It is best described as a compact summary of the leading and disputed problems in the aetiology and treatment of carcinoma of the uterus. Whenever there is discussion of any problem the author gives reasoned opinions and helpfully introduces from the world literature all necessary references. It is strongly recommended that all candidates for the higher examinations in obstetrics and gynaecology should study this book with the greatest care. The sections on the multicentric origin of malignant disease, on stump carcinoma, on the early and late complications of radium therapy, and on the modern methods available for the diagnosis of carcinoma of the uterus in its early stages are all of great interest.

WILFRED SHAW.

PORTRAIT OF HURST

A Twentieth Century Physician. Being the Reminiscences of Sir Arthur Hurst. Foreword by Professor John A. Ryle, M.D., F.R.C.P. (Pp. 200; illustrated. 15s.) London: Edward Arnold and Company. 1949.

It was known to many of us that Hurst was writing his memoirs at the time of his death, and here they are at last, with a charming introduction by John Ryle, who has shared with Lady Hurst the task of reading and arranging the completed chapters. The book begins with Hurst's childhood in Bradford and Manchester and continues fairly fully until 1935, having been interrupted before Hurst could write in detail of the second world war and his last years in Oxford. There are two notable omissions, which are probably to be traced to its unfinished state. The first is the failure to mention Arbuthnot Lane and his school, about whom Hurst's feelings were so strong that perhaps some cooling-off was necessary before they could be recollected in tranquillity. The second is the absence of introspection and of discussion of religion, philosophy, or art. I think Hurst got on well without any belief in the supernatural, but he loved beauty in all its manifestations, in people and in things, and it is odd that he discusses it so little. Indeed, this book will come as a surprise to many who thought they knew him. It reveals an entirely new Hurst. Seeing him there beside us, so often hunched up and silent, one had thought of him as of a mind like Newton's, "forever voyaging through strange seas of thought, alone." Not a bit of it. He was the child among us taking notes, and with the candour of a mirror.

I most enjoyed his account of his undergraduate days at Oxford, as for example the May morning hymn at Magdalen.

"In 1899 Lord Rosebery was at the May morning celebration on the tower with the Dean of Christ Church. It was no great effort for him to be up so early, as he was a life-long sufferer from insomnia and rarely slept after four o'clock."

Or the funeral of Queen Victoria, when Hurst paraded with the Volunteers.

"The coffin, though very heavy, was so short that it only reached from the shoulders of the first to those of the second couple of guardsmen, who had the greatest difficulty in balancing it as they slowly mounted the twenty-odd steep steps into the Chapel. The onlookers were aghast, as it looked as if the coffin would at any moment slide from its precarious position and come hurtling down the steps."

There are equally delightful accounts of Hurst's other great interests, Guy's, the Association of Physicians, and the Medical Pilgrims. Many who knew him in the first world war will turn to his adventures and discoveries then and will be vividly reminded of the scenes they shared together. The one figure they will miss in the picture is Hurst himself, and they will find no word of the disabilities of health from which he suffered. He is like a man who goes on a journey with a camera and takes many photographs, but none of himself. So, in spite of a frank and spirited account of the first fifty years of this century, as seen by a man who was a successful physician and a considerable scientist, the essential reticence is preserved and, like all great men, Hurst remains after all an inscrutable figure.

L. J. WITTS.

STATIC DISEASES OF THE LEGS

Ulcers and Eczema of the Leg. By Holger Bisgaard. Preface by H. Haxthausen, M.D. (Pp. 105; illustrated. No price.) Copenhagen: Einar Munksgaard. 1948.

In Scandinavia the Bisgaard treatment of ulcer and eczema of the legs is established and accepted as being more quickly effective than other methods, and it has the advantage that the treatment is ambulatory. The late Holger Bisgaard, who was a general practitioner, had written extensively on the subject in Danish, and this monograph in English is in effect a résumé of his Danish book.

The treatment consists essentially of massage and movements applied to the foot and the region of the ankle to move the static oedema of these parts. This is followed by careful padding in the hollows below the malleoli, using a "sized" wadding bandage for the purpose. Finally, an elastic bandage is added from the toes to the knee, and applied in such a pattern over the foot and ankle that the maximum pressure is brought to bear upon the sites which hold the stagnant oedema. No one with knowledge of the problem of gravitational disease would doubt the efficacy of such treatment, which will probably receive widespread recognition. In his account of the pathology of these diseases the author appears to be on less sound ground. He describes the static oedema and its sequelae below the malleoli and in the foot as "the infiltration," and to this he attributes much of the evil that arises in these diseased legs, including thrombosis and phlebitis, as well as ulcer and eczema. However, few would deny the material significance of what Bisgaard calls "the infiltration" in the treatment of gravitational disease, and this treatise is to be commended to the notice of general practitioners, dermatologists, and surgeons.

JOHN INGRAM.

Post-traumatic Epilepsy, by A. Earl Walker, M.D. (pp. 86, 28 illustrations; 15s.; Oxford: Blackwell Scientific Publications, 1949), is a short monograph describing the author's experience with 250 patients at a special centre in America. Surgery was reserved for those not controlled by the usual medical treatment. For the localization of the epileptogenic focus electrocorticography was used, and the same method was employed at the end of the cortical resection to make sure that the centre had been removed. The technique is well described. The results show that about half of the patients benefited, but, as the author states, a ten-year follow-up will be necessary to assess the value of operation. The book provides a valuable reference for those who encounter this type of work, though the price seems a little high for the size.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Antibiotics. By H. W. Florey, M.D., F.R.S., and others. Vols. 1 and 2. (Pp. 1174. 168s.) London: Geoffrey Cumberlege. 1949.

Change of Life. By "Medica." (Pp. 76. 5s.) 2nd ed. London: Delisle. 1949.

The Reminiscences of a Physician. By B. Myers, C.M.G., F.R.C.P. (Pp. 159. 10s 6d.) London: H. K. Lewis. 1949.

Arthritis and Allied Conditions. By B. I. Comroe, M.D. Edited by J. L. Hollander, M.D., and others. 4th ed. (Pp. 1,108. 80s.) London: Henry Kimpton. 1949.

Industrial Toxicology. By L. T. Fairhall. (Pp. 483. 46s. 6d.) London: Baillière, Tindall and Cox. 1949.

Heavy Metal Prosthetic Groups and Enzyme Action. By O. Warburg. Translated by A. Lawson. (Pp. 230. 18s.) Oxford: Clarendon Press. 1949.

Occupational Eye Diseases and Injuries. By J. Minton, F.R.C.S. (Pp. 184. 21s.) London: William Heinemann Medical Books. 1949.

A Text-book of Bacteriology for Dental Students. By A. Bulleid, L.R.C.P., M.R.C.S., F.D.S., and C. W. Shuttleworth, L.R.C.P., M.R.C.S., F.D.S. 3rd ed. (Pp. 247. 25s.) London: William Heinemann Medical Books. 1949.

Bermondsey Story. By F. Brockway. (Pp. 246. 15s.) London: George Allen and Unwin. 1949.

Green Thraldom. By Tang Pei-Sung. Introduction by J. Needham, F.R.S. (Pp. 127. 12s. 6d.) London: George Allen and Unwin. 1949.

Bridge's Dietetics for the Clinician. Edited by H. J. Johnson, M.D., F.A.C.P. (Pp. 898. 60s.) London: Henry Kimpton. 1949.

Stillbirths. By I. Sutherland, M.A., F.S.S. Foreword by Professor J. A. Ryle. (Pp. 93. 7s. 6d.) London: Geoffrey Cumberlege. 1949.

The Clinical Management of Varicose Veins. By D. W. Barrow, M.D. Foreword by A. W. Allen, M.D. (Pp. 155. 25s.) London: Cassell. 1949.

Surgical Management of Vascular Diseases. By G. H. Pratt, M.D., F.A.C.S. (Pp. 496. 70s.) London: Henry Kimpton. 1949.

Selected Papers of Haven Emerson. (Pp. 507. $3.) Battle Creek, Mich.: Kellogg Foundation. 1949.

A Textbook of Surgery. By American Authors. Edited by F. Christopher, M.D., F.A.C.S. 5th ed. (Pp. 1,550. 65s.) London and Philadelphia: Saunders. 1949.

Clinical Biochemistry. By A. Cantarow, M.D., and M. Trumper, Ph.D. 4th ed. (Pp. 642. 40s.) London and Philadelphia: Saunders. 1949.

Jordan-Burrows Textbook of Bacteriology. By W. Burrows, Ph.D., and others. 15th ed. (Pp. 981. 45s.) London and Philadelphia: Saunders. 1949.

A Textbook of Physiology. Edited by J. F. Fulton, M.D. 16th ed. (Pp. 1,258. 50s.) London and Philadelphia: Saunders. 1949.

The Eye and Its Diseases. By 92 International Authorities. Edited by C. Berens, M.D., F.A.C.S. 2nd ed. (Pp. 1,092. 80s.) London and Philadelphia: Saunders. 1949.

Operations of General Surgery. By T. G. Orr, M.D. 2nd ed. (Pp. 890. 67s. 6d.) London and Philadelphia: Saunders. 1949.

O Diagnóstico dos Reumatismos. By V. Azambuja. (Pp. 271. No price.) Rio de Janeiro. 1949.

On Post-infectious Nervous Involvement. By F. Möller. Translated by Mrs. J. S. Herrström. (Pp. 187. No price.) Lund: Hakan Ohlssons Boktryckeri. 1949

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SHORTAGE OF Rh TESTING SERA

Supplies of anti-Rh serum are insufficient to satisfy the demands for Rh tests by clinicians in England and Wales. About one-half of the pregnant women in these countries come to term without having an Rh test, and a considerable but unknown proportion of both women and men are transfused without the performance of either an Rh test or a direct matching test adequate to detect Rh incompatibility. Deaths from Rh transfusion reactions continue to occur, and there can be no doubt that many Rh-negative women are still being immunized by transfusion. Many of the latter are thus prevented from ever bearing a viable Rh-positive child. It is plain, therefore, that the demands made for serum are not excessive—they are, in fact, too modest—and some means must be found to augment the supply of serum, apart from the necessity of making the best use of existing supplies.

The difficulties which arise from shortage of anti-D serum serve to illustrate those connected with other sera. Since anti-D serum is essential for testing all mothers and patients requiring transfusion and is also needed for testing donors, it is the serum of which the largest amounts are required. It is fortunately also the commonest variety of naturally occurring serum, but in spite of this the supply does not satisfy half the need. Thus some laboratories are compelled to limit testing beyond a safe limit, and others, particularly hospital laboratories, which should provide an Rh-testing service are unable to do so. Almost the entire supply of anti-D serum used for testing consists of saline-agglutinating (or complete) anti-D serum obtained from D-negative mothers who have been immunized by D-positive foetuses. It has become customary to take ½–1 pint (280–560 ml.) of blood from each mother. A few doctors habitually take larger quantities of blood, which are replaced by transfusion of normal Rh-negative blood. It is only very rarely found possible to obtain serum from males and non-puerperal females immunized by transfusion.

The experimental immunization of male volunteers is being carried out by a few pathologists, but no routine testing serum is known to have been obtained in England by this means. Little if any has been procured by re-stimulation of immunized women who have been sterilized or who have passed the menopause, though useful quantities of serum are being obtained in the U.S.A. by primary immunization or restimulation of volunteers. It must be remembered, however, that a large proportion of such sera contain solely or mainly the albumin-agglutinating or incomplete form of anti-D. About half of the spontaneously produced anti-D is also of the albumin-agglutinating form. At present little use is made of this in Great Britain, but in the U.S.A. much of the testing serum is of this type; it is used either by Diamond's slide method or by tube-testing of red cells suspended in bovine albumin. The latter substance is available in England only in very small quantities, which must mainly be reserved for the testing of sera for the presence of albumin-agglutinating antibodies. Experiments are in progress which may lead to the production in Britain of a similar suspending medium. Meanwhile incomplete antibodies can be used only for testing red cells by suspending the latter in human A B serum or some such colloid as dextran, or by the slide method. Both these methods are apt in inexperienced hands to give rise to false positive results due to rouleaux formation. Hence they cannot be recommended for use by the worker who undertakes Rh testing only occasionally or in emergency, and if they are to be used at all—which may be justifiable because the danger from the occurrence of errors is less than the danger from failing to test those for whom saline-agglutinating serum does not suffice—it must be with a full recognition of their disadvantages.

The other antisera which are required in large quantities are anti-C+anti-D (or pure anti-C) and anti-D+anti-E (or pure anti-E), both of which are needed for the further testing of D-negative donor bloods. Since about one-third of all anti-Rh sera contain anti-C+anti-D, this is the one type of serum of which there is no lack. But in order to avoid giving cdE/cde blood to those D-negative immunized women (and to their babies) who have made anti-E as well as anti-D, all D-negative donor bloods should also be tested with a serum containing anti-E. Pure anti-E sera and anti-D+anti-E sera with a reliable anti-E titre are both rare, and it is therefore unfortunately impossible to test all Rh-negative transfusion blood with such sera. In order to determine the probable Rh genotypes of the husbands of immunized women, and to investigate families where the rarer types of immunization are suspected, it is necessary to use anti-C, anti-c, anti-E, and in some cases anti-e and anti-C^w sera. These are all very rare, especially the last two, and shortage of them seriously limits the genotyping of husbands. Supplies of all these sera are obtained from most of the individuals in whose blood the antibodies have been recognized. They are generally found in the blood of Rh-positive women, and

this probably accounts for many cases being missed, because antibodies are not looked for in the blood of Rh-positive women with the same regularity as in Rh-negative women.

If the benefit of Rh testing is to be given to all those who need it, existing sera must be used with the greatest economy, technicians should be trained in the small-volume technique, and methods for the use of albumin agglutinating anti-D should be developed. But any extension of Rh testing which this may make possible, while most valuable, will be limited, and some way of increasing supplies must be found. Plainly every woman whose serum is discovered to contain antibody of sufficient titre should be persuaded to give a donation of blood if she can do so without injury to her health. The most important single method of increasing supplies of all kinds of anti-Rh sera would be to extend the practice of transfusing women whose blood contains antibodies (including possibly some slightly anaemic ones) with the object of increasing the amount of their donation. Apart from the slight risk of homologous serum jaundice being carried by whole blood, this procedure would be free from danger if the whole operation were to be carried out under the close supervision of the appropriate regional blood transfusion centre. Regional blood transfusion officers are ready and willing to arrange this. Limited but useful amounts of antisera could be obtained by the restimulation of immunized women who have passed the menopause or been sterilized and of immunized males. With proper safeguards this procedure is without appreciable danger. It is already the chief means of obtaining anti-e sera. The value of this method is likely to increase with the passage of time as increasing numbers of women known to be immunized reach the menopause.

There remains the greatest potential source of all, and the most controversial—the immunization of normal male volunteers and of women who have taken vows of celibacy or have passed the menopause. The very great advantage of obtaining sera from such sources must be considered in the light of the attached risks. In time of peace the possibility of emergency transfusion without Rh testing is slight for males living normal lives, but it does exist. For nuns, as well as for males who for religious or other reasons are likely to spend most of their lives in institutions, this risk is negligible in peacetime. In war, however, especially if atomic weapons were used, emergency transfusion would be a definite possibility for everyone, and the transfusion service might have great difficulty in meeting the need for massive transfusions in known immunized persons. Nevertheless, if the other, safer methods of improving the supply of Rh testing sera are not employed, deliberate immunization will have to be considered seriously.

SERUM CHOLESTEROL AND ATHEROMA

The relationship between the level of blood cholesterol and the development of atheromatous arterial degeneration continues to puzzle the experimental pathologist. In 1911 Anitschkow[1] showed conclusively that lesions resembling human atherosclerosis could be produced in animals by feeding them with cholesterol in oil. This did not prove to be a constant finding for other animals, and in fact it is only in the rabbit and chicken that experimental hypercholesteraemia consistently induces atheromatous degeneration. The work of Hueper,[2] however, leaves little doubt that the presence in the blood stream of foreign macro-molecular substances such as polyvinyl alcohol or methyl cellulose does induce a reaction in the blood vessels indistinguishable from atheroma, the foreign material taking the place of cholesterol. Moreton[3] has studied the physical state of the lipids in human subjects with sustained and alimentary hyperlipaemia. By dark-field microscopy and high-speed centrifugation he found that normal serum contains few visible particles and that these resist separation by a centrifugal force of 22,500 G. for one hour. In the serum of patients with sustained hyperlipaemia large colloid particles are visible and readily removed by a centrifugal force of 5,000 G. for one hour. Similar particles were also found in the serum of individuals with alimentary hyperlipaemia, but centrifugation at the same force for 3–5 hours was required for their precipitation. Comparison of the macro-molecular substances used by Hueper with the particles found in hyperlipaemic serum showed that they were similar in size and separability. Moreton therefore concluded that it is the size of the particle which determines the cellular reaction of the tissues to the lymph seeping through the intima from the vessel lumen. For a few hours after each fatty meal particles of the necessary size are present in the circulating blood and presumably in intimal tissue fluid. Particles of neutral fat are locally metabolized or removed, while the more resistant cholesterol accumulates and excites a "foam-cell" reaction. Duff,[4] however, has seriously criticized the view that a flow of fluid normally occurs through the intima from the lumen outwards, and his own experiments have suggested that the main flow of fluid in artery walls is from the vasa vasorum and not from the main lumen.

Leary[5] put forward an alternative suggestion to support the hypercholesteraemic theory of the origin of atheroma. He considers that the cholesterol or other macro-molecules do not enter the lumen by seepage but are carried there by macrophages derived from Kupffer

[1] Anitschkow, N., in Cowdrey, E. V., *Arteriosclerosis—A Survey of the Problem*, 1933, New York.
[2] *Amer. J. Path.*, 1944, **20**, 737.
[3] *Science*, 1948, **107**, 371.
[4] *Amer. J. Path.*, 1932, **8**, 219.
[5] *Arch. Path.*, 1941, **32**, 507.

cells that have taken up the material by phagocytosis. From the sinusoids in the liver these lipid-laden cells enter the systemic circulation, and they then penetrate the arterial intima, the actual sites depending upon local conditions favouring deposition of cells of this size. Gordon[6] suggests as an explanation for the removal of these lipophages from the axial stream that cells of larger size tend to get bumped towards the periphery by the kinetic energy of the moving red cells. Kuntz and Sulkin[7] recently reinvestigated the atheromatous lesions in rabbits that result from cholesterol feeding. The Kupffer cells were marked by indian ink or carmine injections. No ink or carmine appeared in the atheroma foam cells, and they therefore concluded that the lipoid material is not introduced by macrophages derived from the liver but enters the intima in colloidal solution from the lumen. Their view is thus not dissimilar from that of Moreton.

Although the experimental evidence relating to the mechanism by which hypercholesteraemia leads to atheroma is still conflicting, two recent clinical studies strongly suggest a relation in man between hypercholesteraemia and atheroma. Boas and his associates[8] at the Mount Sinai Hospital in New York found that the serum cholesterol was raised to over 300 mg. per 100 ml. in 71 (58%) out of 122 patients with proved coronary atherosclerosis in all of whom the disease began under the age of 50. Only patients with symptoms of coronary artery disease as well as electrocardiographic evidence of myocardial damage were included. The average value of serum cholesterol for the entire group of 122 patients was 316 mg. per 100 ml.; in the 71 patients with hypercholesterolaemia the average value was 365 mg. per 100 ml., and in the remaining 51 patients it was 250 mg. per 100 ml. Other signs believed to indicate disturbed cholesterol metabolism, such as arcus senilis, xanthelasma, and xanthomatosis, were encountered 37 times, mostly in the patients with raised serum cholesterol. In an investigation of the siblings of some of these patients Boas and his colleagues studied 50 families and found hypercholesterolaemia (a serum cholesterol value of 300 mg. per 100 ml. or more) in one-third of the individuals examined. It should be noted that these observations were made mainly on Jews of the private-patient class living in New York. The increased incidence in Jews of other diseases in which the serum-cholesterol level is high—in particular diabetes—is well known, and it would have been interesting to know if high serum-cholesterol values are often found in patients with coronary atheroma who belong to other races. Jewish families in whom coronary atheroma was not recognized might also have been included in the investigation. Stecher and Hersh[9] have also analysed a somewhat similar set of figures. They concluded that the tendency to develop hypercholesteraemia is transmitted as an autosomal dominant gene. If this be so, and if man, like the rabbit, responds to a raised blood cholesterol by formation of atheromatous deposits, then this most common of all arterial diseases must be looked upon in many instances as primarily genetically determined.

It is of course possible that increased serum cholesterol may be an effect of vascular disease, not necessarily a cause. Primary disorders of lipid metabolism are rare: recently the "xanthomatous biliary cirrhosis" of Thannhauser and Magendantz[10] has been demonstrated as secondary to lesions in the liver[11] and can no longer be included with primary lipoidoses. However, if it is finally proved that coronary atheroma is associated with high serum-cholesterol values treatment to reduce the serum cholesterol should be given not only to patients with coronary disease but also prophylactically to siblings who have a raised serum cholesterol. This purpose might be fulfilled by giving a low cholesterol diet, but it is difficult to do this and at the same time keep the diet fully balanced. Moreover, evidence is not conclusive that low cholesterol diets will reduce serum cholesterol. In myxoedema the serum cholesterol is raised, and Turner[12] found that thyroid extract administered simultaneously with cholesterol prevented experimental atheromatosis in rabbits. But patients with angina pectoris and hypercholesterolaemia do not have a depressed basal metabolic rate,[13] and few clinicians would give thyroid extract to patients possibly suffering from ischaemic heart disease. It would be premature to attempt to reduce high serum cholesterol in patients with coronary artery disease without further evidence that it is harmful.

[6] *Arch. Path.*, 1948, **46**, 97.
[7] Ibid., 1949, **47**, 248.
[8] *Amer. Heart J.*, 1948, **35**, 611.
[9] *Science*, 1949, **109**, 61.
[10] *Ann. intern. Med.*, 1938, **11**, 1662.
[11] MacMahon, H. E., *Amer. J. Path.*, 1948, **24**, 527.
[12] *J. exp. Med.*, 1933, **58**, 115.
[13] Davis, D., Stern, B., and Lesnick, G., *Ann. intern. Med.*, 1937, **11**, 354.

PERTUSSIS VACCINATION AND ENCEPHALOPATHY

At a recent inquest (reported in the *Journal* of December 24, 1949, p. 1478) the death from encephalopathy of an eight-months-old infant was ascribed to an idiosyncrasy to pertussis vaccine. Reactions may occur after any form of active or passive immunization,[1] but until recently pertussis vaccination, whatever might be thought of its immunizing capacity, had at least been considered relatively free from side-effects. Madsen,[2] it is true, recorded two examples of fatal convulsions after injection of fluid vaccine in newly born infants, but it seemed likely that age was the precipitating factor. Most of the other reports concerned single

[1] Robinson, L. J., *New Engl. J. Med.*, 1937, **216**, 831.
[2] *J. Amer. med. Ass.*, 1933, **101**, 187.
[3] *Arch. Pediat.*, 1938, **55**, 572.
[4] *Brooklyn Hosp. J.*, 1947, **5**, 107.
[5] *N.Y. St. J. Med.*, 1947, **47**, 1016.
[6] *Pediatrics*, 1948, **1**, 437.
[7] *J. Amer. med. Ass.*, 1949, **139**, 448.
[8] Ibid., 1949, **140**, 555.
[9] Ibid., 1949, **141**, 507.

cases, such as that by Taylor[3] in 1938, so that the incidence of the complication appeared very low and the risk negligible. More recently papers by Brodie,[4] Brodie and Sorley,[5] and Byers and Moll[6] have aroused fresh interest in the subject. The last-named authors record 15 cases of encephalopathy, and the most disturbing feature of their report was that at a subsequent follow-up only one of the surviving children was mentally normal. Two had died of intercurrent respiratory infection, and necropsy on one of them showed diffuse cerebral atrophy and gliosis.

As a result of this report Toomey[7] made inquiries among a number of paediatricians and collected accounts of 38 similar cases. Since he had asked specifically about the occurrence of "convulsions" after pertussis vaccine injections, the series is naturally a mixed one and many of the cases are not fully documented. Nevertheless, he considered that 25 of them were authentic examples of this complication. Byers and Moll had recorded that in three of their cases there was a history either of convulsions in the family or of the infant having suffered previous attacks, and it is interesting to find that in six of Toomey's series similar convulsions had occurred on previous occasions. Toomey does not record the sex distribution, but in the Boston series of 15 cases no fewer than 12 were males. Such findings suggested the possibility of some constitutional predisposition. Brodie,[8] however, has favoured the view that the cause may be an antigen-antibody reaction, though it seems unlikely that this can be the sole explanation, since six of Byers and Moll's cases occurred after the first injection of vaccine. That the condition is not an encephalitis in the strict sense is supported by the necropsy findings in one of the cases recorded by Globus and Kohn,[9] who noted widespread and severe degenerative changes with entire absence of inflammatory reaction.

These findings are disturbing, but to keep the subject in perspective it should be noted that Kendrick, answering Toomey's questionary, reports 20,000 vaccinations with only one convulsive reaction, and that Fraser, of Toronto, has given 300,000 injections without mishap. Nevertheless, it would seem wise to use pertussis vaccine with great caution when there is a family history of neurological disorder; and if the child has had previous convulsions or has any reaction to the first injection attempts at vaccination should be abandoned.

ANTIHISTAMINE RISKS

In a letter to this *Journal* Dr. M. Tobias reported what appears to have been the first death in this country following an overdose of an antihistamine drug.[1] A child aged 21 months accidentally swallowed six 100-mg. tablets of pyranisamine maleate ("anthisan"). Approximately two hours after the child had taken the tablets she lost consciousness. There was a profuse catarrhal discharge from the upper respiratory tract accompanied by epileptiform convulsions. She died three-quarters of an hour after the onset of loss of consciousness. Rives and his colleagues[2] reported similar convulsions in another fatal case. A child of 16 months died fifteen hours after accidentally swallowing 100 mg. of methapyrilene hydrochloride. There appear to have been at least two cases of this kind in France, where the first fatal case was reported in 1947. According to one of the large drug firms, one or two additional cases have also occurred in Britain, but have not yet been reported, one of them in the Bedford area. All these cases emphasize the importance of keeping these tablets out of reach of young children. It should be emphasized, however, that these few fatal accidents, regrettable as they are, must represent a very small proportion of the large number of patients taking antihistamine drugs, the use of which in the treatment of the common cold will be assessed more accurately when the trials arranged by the Medical Research Council have been completed.

[1] *British Medical Journal*, 1949, **1**, 1098.
[2] *J. Amer. med. Ass.*, 1949, **140**, 1022.

HOSPITAL CONTRIBUTORY SCHEMES

Hospital contributory schemes, in one form or another, came into existence soon after the war of 1914–18. Before this the voluntary hospitals had managed to maintain themselves from the resources which they could command from various forms of benefaction. During that war, however, the position changed radically, and in January, 1921, the Minister of Health set up the Voluntary Hospitals Committee (known as the Cave Committee) to examine the financial position of the voluntary hospitals and make recommendations for their assistance. Following the publication of the committee's admirable report, contributory schemes were organized all over the country, some limited to helping one local hospital, others more ambitious, such as those in the big industrial centres of Sheffield, Birmingham, Merseyside, Leeds, and, of course, London, serving groups of hospitals and making provision for the care of their members in whatever hospital they might be received.

The growth of these schemes brought about the inevitable teething troubles, and in 1930 it became obvious that the importance and magnitude of the work were such that some national body was required to which the problems of individual schemes could be brought for solution and through which policy could be discussed and formulated for the movement as a whole. At a conference held in Birmingham in November, 1930, it was decided to form a national association. This was formally established at the first annual conference held in Rugby the following year. The progress of the association, its difficulties, and its triumphs have been admirably described by Mr. A. T. Page in his recently published *Pennies for Health*.[1]

When the hospitals were transferred to the State under the National Health Service Act in July, 1948, it was thought by many that, since the hospitals would thereafter be financed entirely by the State, contributory schemes, and their association, would cease to exist. But the principle of voluntary service has long been one of the cherished ideals of British democracy, and therefore, though the march of events brought about the end of the old association, it brought into existence the new association (1948). This now guides the fortunes of the thirty-four member schemes which had at that time elected to continue their work for the hospital services in new directions, and which will doubtless be joined by many more in the near future. An appendix to Mr. Page's book

[1] *Pennies for Health*. Published by the British Hospitals Contributory Schemes Association (1948).

contains a list of the contributory schemes which are continuing to provide services supplemental to those provided under the Act, together with suggestions for their future activities.

Besides recording the history of the British Hospitals Contributory Schemes Association *Pennies for Health* is at the same time a tribute to the many thousands of people, drawn from all walks of life in all parts of the country, who gave so selflessly of their time and service for the support and maintenance of the voluntary hospitals. By their efforts they raised over £100,000,000 between the first world war and 1947. In the last year of the life of the old association it had 10½ million contributors and achieved a record income of £7,500,000 for hospital and ancillary services.

CONTROL OF BIOLOGICAL WARFARE

During the last three weeks the world has received two reminders that the effective control of atomic weapons, even if this could be achieved, would still leave equally unpleasant alternative methods of human destruction. Mr. Trygve Lie, United Nations Secretary General, deplored that the Atomic Energy Commission, which was entrusted with preparing proposals for the elimination of all weapons of mass destruction, had never discussed biological and chemical warfare.[1] And on Christmas Day the trial opened in the Soviet Far East of twelve senior Japanese officers accused of preparing bacteriological warfare against Russia.[2] According to the indictment, a research station with a staff of about 3,000 was constructed in secret in Manchuria during 1936, and large-scale production was started of the organisms of bubonic plague, typhus, anthrax, and cholera. Fleas were bred in 4,500 incubators, and an apparently successful epidemic of plague was produced experimentally in Southern China in 1941 and 1942. One of the accused, a general in the Japanese Army, gave details of the type of weapons that were designed to spread the organisms. These included small sprays fitted into walking-sticks and fountain pens, but the main agents were to be porcelain bombs dropped from aircraft. American, Chinese, and Russian prisoners of war are reported to have been experimentally infected.

Before the war it was known in Britain that Germany was conducting experiments in bacteriological warfare, and an organization was set up to consider counter-measures. A few months after the Japanese surrender it was disclosed that Britain, the United States, and Canada had been co-operating in energetic research on biological warfare since 1942. The project was an ambitious one—almost 4,000 people were employed for this purpose by the United States Army alone. Among the achievements were the development of methods for the mass-production of organisms and their products, and the isolation and preparation for the first time of a crystalline bacterial toxin. Means were discovered for the rapid and accurate detection of minute quantities of disease-producing agents, for the manufacture of effective toxoid on a large scale, and for protecting clothing and equipment from infection. The attitude of this country to the investigations was clearly defined by the War Cabinet in 1942: "That our principal aim in these studies and experiments was defensive and protective, and that we should, under no circumstances, initiate these forms of frightfulness."

Mr. George W. Merck, United States Government Consultant for Biological Warfare, emphasized in his report of 1946 that the limits of biological attack had by no means been completely measured; and that, unlike the development of atomic energy, the production of effective agents for such warfare was possible without vast expenditure of money or the construction of large factories, and under the guise of legitimate bacteriological research. As pointed out in a leading article in the *Journal*,[3] the technical difficulties of an international control of preparations for biological warfare are so considerable as to make efficient supervision impossible at present. The potentialities of such attack are so great, however, that its prevention deserves some thought even by an organization obsessed with the atomic bomb.

[1] *Scientific American.*
[2] *The Times*, December 28, 1949, p. 5.
[3] *British Medical Journal*, 1947, 1, 893.

NEW YEAR HONOURS

A barony was conferred in the New Year Honours on Dr. Haden Guest for his many services in public life, both in the political arena and outside. He was Labour M.P. for North Southwark from 1923 until 1927, when he resigned from the Party. Later returning to the Labour Party, he was elected M.P. for North Islington in 1937, and has sat for that constituency since then. As chairman of the Medical Parliamentary Group he has been of help to the profession and to medicine in bringing politically non-controversial matters to the attention of the House. Dr. Graham Hodgson, a distinguished radiologist and Director of the *X*-ray Department at the Middlesex Hospital, is deservedly advanced to a knighthood in the Royal Victorian Order. The honours bestowed on Mr. T. E. V. Hurley, Consulting Surgeon to the Royal Melbourne Hospital, and on Mr. T. G. Wilson, Director of Obstetrics and Gynaecology in the University of Adelaide, are timely reminders of the conspicuous part now played by Australia in the advancement of British medicine and surgery. Dr. J. A. Charles, who receives a knighthood, has gained wide experience in public health at Newcastle-upon-Tyne and more recently at the Ministry of Health; he succeeds Sir Wilson Jameson as Chief Medical Officer at the Ministry on May 11. Dr. H. E. A. Boldero stands high in the counsels of the Royal College of Physicians, where he holds the office of Registrar, and he has for fifteen years been Dean of the Middlesex Hospital Medical School. Professor Thomson's knighthood is a welcome acknowledgment of his work for the development of medical science and practice in Northern Ireland, where he has been Professor of Medicine in Queen's University, Belfast, since 1923. In Ceylon, also, the profession has been honoured in the knighthood conferred on Dr. Gunesekara.

Among those honoured outside the medical profession are Sir William Douglas, Secretary to the Ministry of Health, who has probably had a harder time than any of his predecessors in that office; and Mr. Arthur Sims, who, with a munificence necessarily rare nowadays, founded the Commonwealth Travelling Professorship in 1946.

CORTISONE AND ACTH: THE PRESENT POSITION IN AMERICA

BY

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I have recently spent three months in the United States, during which time I had particularly good opportunities of watching most of the clinical and experimental work with "cortisone" and ACTH that is being carried out in the selected medical centres to which these hormones have been allotted for trial.

At the Editor's request, I shall attempt to provide for British physicians a *general and quite simple* account of the work accomplished in America up to the end of November, 1949. This is not easy, for many of the things seen or heard, both clinical and experimental, are as yet unpublished; and it would manifestly be wrong to describe them in detail or even to refer to some of them at all. Nevertheless a general account may be welcome, since knowledge of what is going on is still fragmentary in Britain.

The first part of my visit, so far as cortisone and ACTH are concerned, was mainly devoted to clinical observation of many patients in hospital under short-term treatment with one or other of the two substances. The patients seen included not only sufferers from the rheumatic diseases, on which Hench's original and dramatic discovery was made at Rochester (Mayo Clinic), but also sufferers from a wide variety of other diseases, both acute and chronic. During later weeks I took greater interest in the work going on feverishly at the selected centres on the important problem of how these hormones act, and how they (or other related compounds) may ultimately be harnessed for use in practical therapeutics.

The immediate effects of cortisone in rheumatoid arthritis were so dramatic that almost all the tremendous publicity, especially in the lay press, has been devoted to the hope that a cure has at last been found for this one serious and chronic disease. This position is no longer correct, for as soon as cortisone (or ACTH, which acts indirectly but similarly) had been tried out in a wide variety of other diseases, acute and chronic, immediate and astonishing results were seen to occur in a number of them.

It was then realized that something quite new and fundamental in medicine and therapeutics had been discovered, with far wider possibilities and implications than had at first been conceived. It is not too much to say that the problems of cortisone and its action in the body now extend far beyond the boundaries of the chronic rheumatic diseases, in which its remarkable effects were first demonstrated.

The Two Hormones—Cortisone and ACTH

Cortisone is, so far as we know at present, the essential substance involved in this new discovery, and it is necessary to explain how ACTH comes into the picture at all.

Cortisone is one of the steroid compounds, now accepted as a hormone, which had been shown to exist in the suprarenal cortex, and its structural chemical formula had been established. It is present, however, in such small amount that a supply sufficient to test its physiological actions completely was never obtainable from the suprarenal cortex. The cortisone now used clinically and experimentally is entirely a laboratory product, identical in chemical structure with the natural suprarenal secretion, and built up by Kendall in 1938 by a long and difficult synthetic technique using bile acids as his starting-point or source. Kendall named his synthetic substance "compound E," and for ten years it lay simply as a chemical triumph until his colleague Hench, on good theoretical grounds which he has well described, first tried it in a patient suffering from rheumatoid arthritis. All the cortisone (compound E) now available in the United States is made by Merck and Co., Inc., essentially by Kendall's process, using bile acids from ox bile as the source.

ACTH, or pituitary adrenocorticotropic hormone, is a natural product obtained from the pituitary glands of animals, chiefly pigs, and has not been made synthetically. Its preparation is not unduly troublesome for the expert chemist, but it seems difficult to ensure an end-product which is both active and pure. ACTH first became available in adequate amount for clinical investigation in 1948, in the autumn of which Hench actually began his work with cortisone in rheumatoid arthritis. It is now evident that the physiological function of ACTH is to stimulate the secretory activity of the suprarenal cortex, and the hormone was first used to advantage by Thorn and his colleagues in Boston as a test of suprarenal function in Addison's disease.

It is now clear that stimulation of the suprarenal cortex by ACTH induces an increased secretion of cortical steroids, including the all-important cortisone. So long as the suprarenal cortex is functionally intact, therefore, administration of ACTH merely excites an increased production of cortisone, and the clinical results are, theoretically at least, essentially the same.

The chief but not the sole supplies of ACTH used in America have come from the laboratories of Armour and Co., Chicago, the well-known meat-packing firm, to whom abundant hogs' pituitary glands are available.

To reiterate, for clearness. An increased amount of cortisone in the body, capable of inducing the clinical effects observed, can be brought about in two ways: (1) directly, by parenteral injection of synthetic cortisone, and (2) indirectly, by parenteral injection of ACTH, which stimulates the suprarenal cortex to secrete more cortisone.

One interesting point that may be of great importance in connexion with what are termed "side-effects" should be mentioned here. Injections of synthetic cortisone do not stimulate the suprarenal cortex—on the contrary, it has been suggested that they may "put it to sleep," at least for a time. ACTH, on the other hand, increases the natural production of cortisone and other steroids by the suprarenal cortex, and its continued use might lead to hypertrophy and uncontrolled hypersecretion.

Before leaving the description of the two hormones it should be stated that the American supplies of cortisone and ACTH, from Messrs. Merck and Co. and Armour and Co., respectively, have all been given free of charge to the carefully selected experimental centres; but it is clear that this arrangement cannot continue indefinitely, and may indeed very soon terminate.

Clinical Effects of Cortisone and ACTH

As just explained, the administration of each hormone gives rise to an immediate increase of cortisone in the body—in one case directly, in the other indirectly. The result is essentially the same; and since far more ACTH has been available, owing to its easier production, many more patients have been tested and treated with this hormone than with synthetic cortisone.

The rapid and intensely dramatic effects with each hormone in rheumatoid arthritis, first discovered by Hench and his colleagues, have already been adequately described in British journals. To me the most extraordinary thing was the speed of the improvement, with relief both of pain and of stiffness, and also, alas, the pathetic rapidity of relapse when treatment was stopped and replaced by injections of inert colloidal cholesterol in identical containers. The almost immediate euphoria and mental stimulation in the patients is equally remarkable, and there are now good reasons for believing that this is not just an ordinary psychological effect but if kept going by continual treatment may in rare cases end in acute psychosis.

The whole effect of this treatment in rheumatoid arthritis was aptly described by an American friend as "like suddenly turning off the tap and then (when hormone treatment is stopped) suddenly turning it on fully again." I saw no case of rheumatoid arthritis completely or permanently cured with cortisone or ACTH. Short courses of treatment, given at intervals, have, however, led to considerable lasting improvement over a number of months. It should be noted that scarcity of the two active hormones was not the only cause of the short periods of treatment, but also the undesirable "side-effects," which are described separately below.

I have seen the effects of cortisone and ACTH in a wide variety of diseases, chiefly medical but a few surgical. I observed immediate or rapid beneficial effects—probably as great but not so visibly dramatic as in a crippling disease of locomotion such as rheumatoid arthritis—in acute rheumatic fever, chorea, gout, chronic ulcerative colitis, lupus erythematosus diffusa, scleroderma (with oesophageal involvement), asthma, lymphadenopathies (including lymphosarcoma and Hodgkin's disease). I have heard of, but did not see, other diseases in which great improvement was obtained. Unfortunately, except on a second visit to Boston after an interval of several weeks, I was unable to follow the progress of many patients for an adequate time. I am therefore unable to state how many of the patients seen in the early stages of treatment subsequently relapsed, or if any were permanently cured as a result of the hormone therapy. I have no doubt that in one patient, suffering from acute lupus erythematosus and obviously at death's door, the effect of cortisone was absolutely life-saving. I cannot say, however, whether this patient has remained well or has subsequently relapsed.

One fact concerning the clinical action of cortisone (and ACTH) has already been touched on in American publications and may be mentioned here as of interest to surgeons as well as physicians. Wounds show no sign of healing and abscesses no signs of granulation-tissue formation in patients (or animals) to whom the hormone is being administered. The possible fundamental implications of this important observation are discussed below, but it seems obvious that this effect might be good (for example, in inflammatory diseases of joints, etc.) or disastrous (for example, on the granulation-tissue barrier round an active tuberculous lesion).

Side-effects of Cortisone and ACTH

I saw undesirable side-effects in a considerable number of patients treated with cortisone or ACTH, but none was severe and most of them seemed in process of passing off after treatment had ceased. I heard of serious side-effects, including persistent hypertension, glycosuria and even true diabetes, acute spread of tuberculosis, and violent mental disturbance. I can say nothing about these except to express a hope that, if true, accounts of them will soon be published.

By far the commonest side-effect seen by me with both hormones was a very modified Cushing's syndrome, characterized by "moon-face," acne, rapid gain in weight, hirsuties in females (seldom more than trivial), and striae of the skin. This side-effect was not to be wondered at, and indeed was almost to be expected in view of the well-known association of hyperactivity of the adrenal cortex with Cushing's syndrome. While relatively benign and unimportant, following *short* courses of treatment, it seems evident that the early development of this syndrome may preclude, until our knowledge increases, administration of cortisone or ACTH over long periods of time.

A few side-effects described may be due to other pituitary hormones being present in some samples of ACTH, but these should be avoidable in future.

How do Cortisone and ACTH Act in the Body?

It is far too early to attempt any real answer, and the most active and energetic research work, both in patients and in animals, is being pursued at a number of centres in the United States.

A few positive indications have already emerged, the most important suggestion being that cortisone has some governing or controlling action on the so-called collagen tissues (including connective tissues and scar tissue) and lymphoid tissues of the body. The full evidence in favour of this view has not yet been published; but what has already been said here about the clinical effects on the fibrous tissues in rheumatoid arthritis, on the prevention of wound-healing, and on the remarkable results in lupus erythematosus diffusa (a so-called collagen disease) is sufficient to indicate a promising line of research, which also lends itself to animal experiments.

Many complete and elaborate metabolic investigations have already been carried out on patients under treatment, some of which have been published. Nothing, however, indicating any constant and important chemical change in body metabolism has been discovered, but only some fresh knowledge of various side-effects—for example, glycosuria.

Quite a different line of research, which has already attracted great attention, arises from the work of Hans Selye and his colleagues in Montreal, Canada. Selye's recent paper in this *Journal* (November 19, 1949, p. 1129) on the "Participation of the Adrenal Cortex in the Pathogenesis of Arthritis" gives details of one part only of his researches. Selye's main hypothesis or generalization has been gradually shaping itself over a period of years as his "general-adaptation syndrome." He suggests that following exposure to a great number of "stresses" (emotional tension, infections, intoxications, etc.) the body may respond with increased production of adrenal cortical hormones, which help to raise general resistance. This general-adaptation mechanism may, however, go wrong and, on Selye's hypothesis, of itself become a principal cause of disease, including the rheumatic and the so-called collagen diseases. It is interesting to hear physicians in America already talking of "stress diseases," but it must be remembered that Selye's work simply puts forward a hypothesis, the proof of which must, as always, depend on how it fits all the facts.

Some Conclusions

1. The discovery of the clinical effects of cortisone (and ACTH) is something of quite fundamental importance in medicine, the ultimate implications of which, in the prevention or treatment of disease, cannot yet be foreseen.

2. No one knows how cortisone works. All we can say is that, thanks to the work of Hench and Kendall, we have been provided with a new and powerful weapon for medical research, the results of which may take a long time to gather fully.

3. The effects in the chronic rheumatic diseases are dramatic; and Hench, in a public lecture in Boston, described the discovery of cortisone as the "end of the beginning" of hope for sufferers from rheumatoid arthritis. This is true, but is as far as we should go at present, and uninformed but understandable publicity is to be deplored.

4. A number of other diseases, mostly chronic but some acute, show almost as striking immediate improvement when cortisone or ACTH is administered.

5. It is clear that both cortisone and ACTH are at present a long way removed from ordinary therapeutics, for they have unavoidable dangers as well as beneficial effects. Their practical application must await the results of intensive research.

6. Bile acids are at present the only source from which cortisone can be made commercially, and so long as this is so the hormone will always be very scarce and very expensive. It is well known that search for cheap and abundant vegetable "sources" is now going on in many parts of the world.

Meanwhile the chemists are not idle; and in conversation with some of the steroid chemists in the United States I gained the impression that they are not excited by these expeditions, but are confident that some simpler substance will be found having the same effects as compound E.

I wish to thank many medical friends in the United States who so willingly showed me their patients and discussed their problems, especially Drs. Bauer, Keefer, Thorn (Boston); Baehr, Loeb (New York); Hench, Kendall (Rochester, Minn.); Harvey, Marshall, Rich (Baltimore); Carlisle (Merck and Co.); Mote (Armour and Co.); and Sevringhaus (Hoffmann-LaRoche, Inc.).

MEDICAL NEW YEAR HONOURS

The names of the following members of the medical profession were included in a New Year Honours List published in the *London Gazette* on January 2.

Baron

LESLIE HADEN GUEST, *M.C.*, M.R.C.S., L.R.C.P., M.P. Member of Parliament for Southwark North from 1923 to 1927, and for Islington North since 1937. For political and public services.

K.C.V.O.

HAROLD KINGSTON GRAHAM HODGSON, C.V.O., M.B., B.S., F.R.C.P., D.M.R.E., F.F.R., Director of the *X*-ray Department, Middlesex Hospital.

K.B.E. (Civil Division)

THOMAS ERNEST VICTOR HURLEY, C.B., C.M.G., V.D., M.D., F.R.C.S., F.R.A.C.S., Melbourne, Victoria, Australia. For public services.

Knighthood

HAROLD ESMOND ARNISON BOLDERO, D.M., F.R.C.P. Dean of Middlesex Hospital Medical School and Registrar of the Royal College of Physicians of London.

JOHN ALEXANDER CHARLES, M.D., F.R.C.P., D.P.H., at present Deputy Chief Medical Officer, Ministry of Health. Will succeed Sir Wilson Jameson as Chief Medical Officer of the Ministry of Health and of the Ministry of Education on May 11.

FRANK ARNOLD GUNESEKARA, C.B.E., E.D., M.R.C.S., L.R.C.P., Senator, Ceylon.

WILLIAM WILLIS DALZIEL THOMSON, M.D., F.R.C.P. Professor of Medicine in Queen's University, Belfast.

THOMAS GEORGE WILSON, C.M.G., M.D., F.R.C.S.Ed., F.A.C.S., F.R.A.C.S., F.R.C.O.G. Director of Obstetrics and Gynaecology, University of Adelaide, South Australia. For public and philanthropic services.

C.B. (Military Division)

JOSEPH ARCHIBALD MAXWELL, C.V.O., C.B.E., F.R.C.S.Ed., Surgeon Rear-Admiral, R.N.

FRANCIS ROBERT HENRY MOLLAN, O.B.E., *M.C.*, L.R.C.P.&S.I., Major-General, late R.A.M.C.

TERENCE CHARLES ST. CLESSIE MORTON, O.B.E., M.D., F.R.C.P., D.P.H., D.P.M., D.T.M.&H., Air Vice-Marshal, R.A.F., Honorary Physician to the King.

C.M.G.

ERIC HOWARD MANLEY LUKE, M.B., Ch.B. A surgeon at Wellington Public Hospital, New Zealand, for over 25 years and Chairman of the Council of the New Zealand Branch of the British Medical Association.

C.B.E. (Military Division)

THOMAS NORMAN D'ARCY, L.R.C.P.&S.I., D.O.M.S., Surgeon Captain, R.N.

ANDREW HARVEY, M.B., B.Ch., D.P.H., Group Captain, R.A.F.

C.B.E. (Civil Division)

JANET KERR AITKEN, M.D., F.R.C.P., Consulting Physician, Elizabeth Garrett Anderson Hospital. Member of the Council of the Royal College of Physicians of London.

ROBERT VIVIAN BRADLAW, F.R.C.S., M.D.S., F.D.S. R.C.S., Dean of the Faculty of Dental Surgery, Royal College of Surgeons of England; Professor of Oral Pathology in the University of Durham.

CLIFFORD VINEY BRAIMBRIDGE, M.V.O., M.B., B.Chir., F.R.C.S.Ed., Colonial Medical Service. Senior Surgical Specialist, Kenya.

IDA CAROLINE MANN, D.Sc., M.B., B.S., F.R.C.S., D.O.M.S., Senior Surgeon, Royal London Ophthalmic Hospital.

ERNEST ALEXANDER NICOLL, M.D., F.R.C.S.Ed., Surgeon-in-charge, Berry Hill Hall Miners' Rehabilitation Centre, and Consulting Surgeon to the Miners' Welfare Commission.

FREDERICK TAVINOR REES, *M.C.*, T.D., M.R.C.S., L.R.C.P., Director-General of Medical Services, Ministry of Pensions.

O.B.E. (Military Division)

ALFRED EDWARD FLANNERY, L.R.C.P.&S.I., Surgeon Commander, R.N.

O.B.E. (Civil Division)

OKUNADE AJIBADE, L.R.C.P.&S.Ed. For public services in Nigeria.

EDGAR SCOTT BOWES, M.R.C.S., L.R.C.P., Chairman, Poole Centre, St. John Ambulance Association.

THOMAS GREGORY BURNETT, M.B., Ch.B., Chairman, Bulawayo Hospital Advisory Committee, Southern Rhodesia.

ERNEST THOMAS CONYBEARE, M.D., F.R.C.P., Medical Officer, Ministry of Health.

PANAGODAGE BERTRAM FERNANDO, M.B., B.S., M.R.C.P., Professor of Medicine in the University of Ceylon.

ROBERT SEARSON RODNEY FRANCIS, M.B., Ch.B., of Hastings, New Zealand. For services to the community in connexion with the treatment of tuberculosis.

MINNIE GOSDEN, M.B., B.S., Colonial Medical Service. Senior Pathologist, Sierra Leone.

GEORGE VERT THOMSON MCMICHAEL, M.B., Ch.B., D.P.H., Medical Officer of Health for the Burgh of Paisley.

DAVID GWILYM MORGAN, M.R.C.S., L.R.C.P., Administrative Medical Officer, United Cardiff (Teaching) Hospitals.

ARTHUR HAROLD MORLEY, M.B., Ch.B., F.R.C.S.Ed., Colonial Medical Service. Surgical Specialist, Tanganyika.

CHARLES ELIAS REINDORF, M.D. For public services in the Gold Coast.

ALFRED EATON SPAAR, F.R.C.S.Ed., Medical Practitioner, Kandy, Ceylon.

JOHN HARGREAVES HARLEY WILLIAMS, M.D., D.P.H., Secretary-General, National Association for the Prevention of Tuberculosis.

M.B.E. (Military Division)

MOHANDIRANGE DON SIMON JAYAWARDENA, E.D., L.R.C.P.&S.Ed., Major, Ceylon Medical Corps (Reserve).

Sir William Scott Douglas, K.C.B., K.B.E., Secretary of the Ministry of Health, has been promoted to G.C.B.

The King intends to confer the honour of Knighthood on Mr. Arthur Sims "for services to medicine and education in the British Commonwealth." In 1946 Mr. Sims made a gift of 10,000 £1 Ordinary Shares of Cooper, Triffitt and Co., Ltd., to the Royal College of Surgeons of England for the endowment of a Commonwealth Travelling Professorship, providing an income of £2,000 a year. In 1948 Sir Hugh Cairns was appointed the first Travelling Professor and was followed by Professor G. W. Pickering (1949) and Sir Reginald Watson-Jones (1950).

REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE EARLY DIAGNOSIS OF BRONCHIAL CARCINOMA

BY

R. C. BROCK, M.S., F.R.C.S.

Thoracic Surgeon to Guy's Hospital; Surgeon to the Brompton Hospital

A generation ago bronchial carcinoma was a rare disease; this is far from the case to-day. All practitioners have been brought up to a knowledge of carcinoma of the stomach and of the colon, and have been taught to think of and look for these diseases. The incidence of bronchial carcinoma in men is to-day very little different from that of carcinoma of the stomach or colon, and it is therefore evident that it is a disease that demands equal attention. Furthermore, a bare 16 years ago bronchial carcinoma was virtually incurable; its diagnosis was synonymous with a death-warrant. Since Graham demonstrated in 1933 that pneumonectomy could be performed successfully for its treatment we have had this means at our disposal. Graham's original patient is still alive and working, and a sufficient number of other patients have survived for 5 to 10 years or longer to prove beyond doubt that the condition is now definitely curable in a proportion of cases.

Improved Outlook

In the early years of surgical treatment the operability rate was low and the mortality of operation relatively high. The operability rate is now much higher and the mortality rate from operation much lower. For instance, analysis of my own figures from 1942 up to the end of 1948 reveals the following encouraging improvement.

Cases of Bronchial Carcinoma, 1941–8

Total seen	800
Thoracotomy	172
Inoperable at thoracotomy	59
Operable	106

Average operability = 13.25%

Last Four Years; 449 Cases, 83 Operable = 19%

1945	15%
1946	13%
1947	21%
1948	23%

There have been 19 deaths in 136 operations for removal of growth. In the last 100 cases there have been 9 deaths, and only 2 operative deaths in the last 40 cases, both of which were bad risk cases.

The improved operability rate is due in some measure to improved technique. Increased familiarity with the problem and increased confidence enable one to operate on cases that earlier would have been thought entirely unsuitable. Apart from this, there is no doubt that the improved operability rate is also due to patients being sent earlier for diagnosis and for treatment. The surgeon can cure many cases of bronchial carcinoma, but only if the patient is referred to him in a favourable phase of the disease. The main task in this matter lies with the general practitioner and the consultant physician, who must inevitably see the patients first, for no patient will direct his own steps to the thoracic surgeon.

Practitioners are becoming increasingly "carcinoma-of-the-lung-minded" and are referring many more patients for advice and treatment at an early phase of the disease. This is a healthy sign, and deserves the proper recognition due to it. In fact, in the larger chest centres the steady stream of cases of bronchial carcinoma is tending to be embarrassingly large in face of the great difficulty in providing beds for cases of all sorts that has resulted from the steady, and as yet apparently unchecked, deterioration of the bed situation.

Principles in Diagnosis

The most important factor in making a diagnosis of a disease is to think of the possibility of its existence. It is a sound general rule to state that any departure from normality in the functions of any viscus or major structure in the body in a patient of cancer age should make one think of the possibility of malignant disease. If this is borne in mind in the case of the lungs we should have far fewer examples of gross delay or complete oversight in the diagnosis of bronchial carcinoma.

In some early cases it is extremely difficult to diagnose the condition, even with good radiology. In a number of cases no one but an expert should feel that he has been at fault in not making an earlier diagnosis. Of much more practical importance is the large number of patients still seen who have been under observation with empirical treatment for several months, and who are found to be inoperable when they eventually attend for special examination. In a great proportion of these cases the diagnosis would have been made much earlier if the significance of certain simple features had been recognized. It is therefore of chief importance for us to consider these aspects rather than the more complex and difficult presentations that may deceive or perplex even the expert.

It should be remembered that the average duration of life from the time the patient first presents himself for treatment is somewhere between six and nine months. It follows that it is useless to spend three to four months or more in making a diagnosis and then to expect the disease to be curable in any but a very small proportion of cases.

One of the gravest errors, which all teachers should concentrate on stamping out, is the impression, still far too prevalent, that a diagnostic feature is that the patient should look as if he had got cancer, or at any rate some grave disease. We no longer expect to see a typical "consumptive" before we think of diagnosing pulmonary tuberculosis. We should know that if at a glance the patient looks likely to have malignant disease then he is almost certainly past all hope. We are then looking at the picture of approaching death, not of malignant disease (Fig. 1). This applies to cancer any-

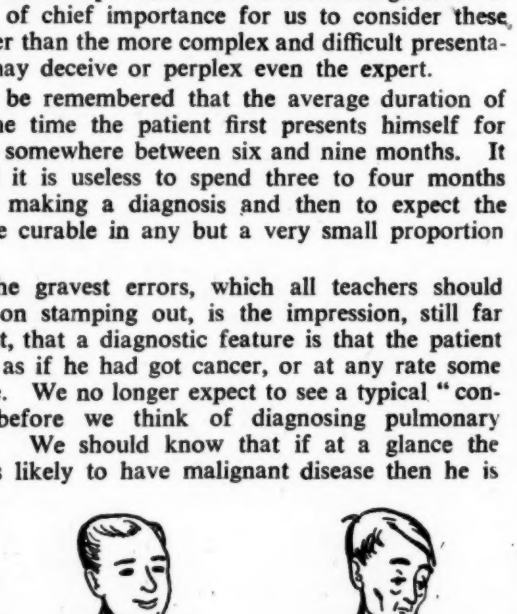


FIG. 1.—The general well-being of the patient with an early growth is contrasted with the cachexia in advanced disease.

where, but demands special emphasis in connexion with bronchial carcinoma. One still hears statements that the clinical features or radiological appearances are consistent with carcinoma but the patient does not "look as if he has got a growth." Such an attitude to-day is stupid, ignorant, and almost contemptible. By all means use the appearance of malignant cachexia as a diagnostic point if, unhappily, it is there—but do not wait for it to appear before thinking of cancer.

Symptoms

Unfortunately, carcinoma of the lung, like that of other viscera, is at times so insidious in its onset or so swift in its course that the earliest clinical manifestation may be that of a mortal extension or complication. The first symptom may, for instance, be due to a cerebral metastasis. For these cases no one can upbraid himself.

Bronchial carcinoma is commonest between 40 and 60, but may appear at any age. It must be thought of in the thirties, and is by no means infrequent in the twenties. Unfortunately in these younger people it is rarely amenable to successful treatment. It is four times as common in men as in women.

Cough.—By far the most important symptom is cough. The onset of cough in a middle-aged patient hitherto free from the symptom is always most suggestive. Very often the cough is dry and rather insignificant, and is ascribed to smoking or passed over as of little or no importance. Even when a symptom such as blood-spitting causes the patient to seek advice he may still make light of any pre-existing cough. I have found that direct inquiry from the wife usually reveals a more reliable story. In a fair proportion of cases, on the other hand, one finds that the patient says he has had a cough for many years and that he has noticed no change in it, though some will remark upon a recent change in its character. Here again the wife may prove to be the better informant. A not uncommon feature is that the usual winter cough that the patient may have suffered has not cleared up in the summer and has been associated with new symptoms.

Haemoptysis.—The most significant symptom and the one which so often sends the patient to his doctor is blood in the sputum. This is a most important feature, and the patient should always be carefully cross-examined about it. The blood is often so small in amount as to disarm suspicion in an easy mind, and its very persistence may allay anxiety, especially if the patient is reassured by his doctor. Patients may be so unreliable in their evidence—and this can be such valuable evidence—that in every suspicious case the sputum should be inspected by the doctor. Pink discoloration is often found when bleeding has been denied. Continuous daily, or almost daily, blood-staining of the sputum extending over weeks or months is, from the practical standpoint, diagnostic.

Pain.—Pain is not a common feature and does not often cause the patient to seek advice, unless it be from bony metastases or from an acute pleurisy. More often there is only a dull ache or a sensation of discomfort.

Symptoms of Secondary Infection.—The pain of acute pleurisy naturally leads to consideration of the next most common manifestation of the disease—namely, those features due to secondary infection behind the growth. In their milder forms they are diagnosed as "bronchitis," "pleurisy," or "influenza," and in their more severe forms as "pneumonia" or "fluid." An empyema or a lung abscess may also occur. All or any of these may be legitimate diagnoses; their sinister significance lies in their imperfect resolution or their recurrence.

One of the commonest complaints is that of the man who has never felt the same since his attack of "flu" last winter, whose cough has persisted or whose symptoms have recurred with increased severity after temporary improvement. "Unresolved pneumonia," often a radiologically inspired diagnosis, must always lead to the gravest suspicion of cancer, and every effort must be made to exclude it.

In the past the classical diagnoses of "pleurisy" and "pneumonia" were so honourable as to be accepted as complete in themselves. In many cases these illnesses are symptoms rather than primary diseases, and we should not rest until we have excluded an underlying major causal lesion. Every patient who has had "pneumonia" should certainly be examined radiologically in convalescence.

Even the occurrence of an empyema after an attack of pneumonia should not allay suspicion, but a routine consideration and exclusion of growth should be made.

"Lung abscess" is often another trap. It should be remembered that after the age of 45 there is a one-in-three chance of a lung abscess being due to a growth of the lung.

Apart from these inflammatory manifestations, bronchial carcinoma may present, especially in the elderly, as an insidious disease causing only vague deterioration of health with lassitude, loss of weight, and anaemia. Indeed, the quiet deterioration may lead to suspicion of a concealed carcinoma of the stomach and a shadow in the lungs may be revealed incidentally in the course of a screen examination for this condition.

Clinical Examination

Unreliability of Physical Signs.—Physical examination of the chest may reveal some obvious abnormality, but it will often show nothing at all, or nothing that is diagnostic. It cannot be too strongly emphasized that the placing of faith in percussion and auscultation is absolutely wrong: a negative examination means nothing. Only by good radiology can an early diagnosis be made in most cases.

There are only two physical signs that point strongly to growth. One of these is absolute dullness not due to fluid and the other is bronchial stridor. Both of these are more likely to be noted in advanced or hopeless cases.

Radiology.—Radiology is our chief means of diagnosis, but it must be good radiology. A technically poor film may cause a growth to be overlooked, and there are still far too many poor radiographic apparatuses about to-day. Moreover, although at times the radiologist may be able to say definitely and correctly that the patient either has or has not got a growth, in general it should be recognized—by radiologists as well as clinicians—that in many cases all he can say is that there is an abnormal opacity within the chest. This observation having been made, further full investigation is needed.

Lymphatic Glands.—Before considering bronchoscopy I must emphasize the need for a simple but nevertheless meticulous examination of the lymphatic glands and the abdomen. It is surprising how often one is asked to see a patient who has been under observation for many months and in whom no final diagnosis has been made, yet palpation of the neck reveals enlarged hard glands that show the diagnosis was literally at one's finger-tips if one used them properly (Fig. 2). In this way a correct diagnosis may often be made in a few seconds.

Clubbing.—The diagnosis may also be literally at the finger-tips in another manner. Well-marked clubbing of the fingers can in itself be a final diagnostic feature if noted in connexion with a chest illness of short duration

FIG. 2.—Careful examination for enlarged glands.

in a middle-aged patient—always, of course, excluding a simple overlooked empyema (Fig. 3).

Bronchography and Bronchoscopy.—Bronchograms should not precede bronchoscopy. There is a temptation to do this, perhaps because a bronchogram may be done more easily than a bronchoscopy. It is seldom diagnostic and is often confusing or ruins the radiological picture for months. In any suspicious case bronchoscopy is indispensable, and if it is not procurable locally the patient should be referred to one of the many chest centres now about the country, where expert bronchoscopy can be carried out. Bronchoscopy not only provides exact diagnosis, including biopsy in a good proportion of cases, but is also valuable in assessment of operability.

Barium Swallow.—In this connexion it is not possible to avoid mentioning another simple investigation that is more often than not omitted, which is often conclusive, and which should never be dispensed with—barium examination of the oesophagus. If this is done, again with meticulous care, and in addition to screening radiographs are taken for leisured study and record, evidence of mediastinal involvement will often be revealed. The opacity due to the growth so often blends with the mediastinal shadow, making it impossible to assess its medial configuration. Contrast radiography with barium will enable this demarcation to be done (Fig. 4). Again, as with overlooked glandular involvement, one finds that this examination provides at once the information to make a diagnosis not only of growth but, unfortunately, of inoperability as well.

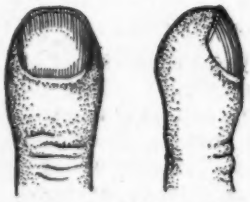


FIG. 3.—Well-marked finger clubbing is often a diagnostic feature.

Indications for Radiology.—There remains the question of how often one is justified in submitting patients to radiography when some relatively minor chest symptom is present. It is clearly not practicable to have every patient with a cough radiographed. Clinical judgment on the part of the doctor is essential in this selection, and it must be emphasized that it is the change in character of a cough or its failure to resolve rapidly under simple treatment that should lead to *x*-ray examination.

It should be possible to increase greatly the facilities for *x*-ray examination of the chest, and this should be one of the earliest duties of the health authorities. Since 1942 the Bermondsey and Southwark health authorities in the district around Guy's Hospital have encouraged doctors to send for radiography any patient presenting any chest symptoms. In this way, apart from the discovery of other chest diseases, many cases of bronchial carcinoma have been detected at a much earlier and more favourable phase than would otherwise have been the case. Unfortunately, even this policy does not ensure a high proportion of operable cases, but it is incontestably sound and should be widely followed.

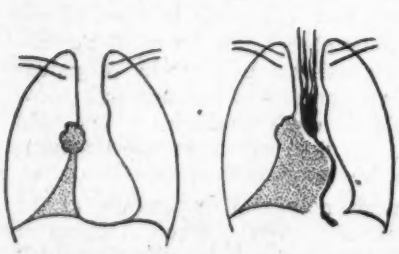


FIG. 4.—Barium examination of the oesophagus may reveal extensive mediastinal involvement.

The first essential for early diagnosis is for the doctor always to bear in mind the possibility of the condition and so apply his clinical ability to discover the suspicious case. The next is the access to good radiology. Reference to a special thoracic unit for completion of the diagnosis and final assessment should then follow naturally.

The illustrations in this article were drawn by Miss S. Treadgold, of the Department of Medical Illustration, Guy's Hospital.

LONDON'S HEALTH SERVICES

TRANSITION PHASE OF 1948

The changes which took place in the health services of the London County Council in the middle of 1948, with the coming into operation of the National Health Service Act, provide the opening theme of the recently issued[1] report of the County Medical Officer of Health. Overnight the Council said farewell to its 98 municipal hospitals, and at the same time it welcomed the maternity and child welfare services, the vaccination and immunization services, and the tuberculosis care and aftercare services of the Metropolitan boroughs. The transition was effected with such smoothness that the patients in hospital beds on July 4–5 and the women attending clinics were all unaware of any change in the administrative structure. London now comprises nine health divisions, each with a medical officer in charge. One day it will comprise 162 health service areas, each, it is hoped, with a comprehensive health centre.

The year 1948 was a very healthy one for London. The general death rate (11.1 per 1,000 population), the infant mortality rate (31 per 1,000 live births), and the maternal mortality rate (0.77 per 1,000 live and still births) were the lowest recorded. Of London boroughs Lewisham and Kensington had the lowest death rate, Bermondsey the lowest infant mortality rate (16 per 1,000), and Chelsea the highest (40).

There were lowered mortality rates for almost all the principal causes of death, but deaths from cancer showed a slight rise for the second year. In London the cancer mortality is higher than in England and Wales as a whole. It is, however, not as high as a misprint in Table 4 would make it appear. This Table gives 7,915 as the number of deaths of females from cancer in "all other sites" (than the four specified), compared with 2,713 for males; the figures for females should be 1,915.

Mortality rates for all the respiratory diseases were very low, and there were further falls in the notification rates for infectious diseases, except in the case of measles. Scarlet fever, which fifty years ago caused 1,000 deaths annually in London, caused only two in 1948, and the deaths due to whooping-cough are only one-thirtieth of what they were at the beginning of the century.

The fall in the incidence of diphtheria reflects the success of the immunization campaign. In 1938 there were 205 deaths from diphtheria at all ages, and in 1948 only 19. The total number of children under 15 who died as a result of diphtheria, measles, influenza, acute poliomyelitis, and polio-encephalitis combined was almost the same as the number of children who died as a result of traffic accidents on the road.

The morbidity figures for pulmonary tuberculosis are still more than 20% higher than before the war, but how far this is due to increased zeal in seeking out cases cannot be assessed. Of the 6,000 primary notifications of all forms of tuberculosis in 1948, 1,265 were for persons of 45 and over.

[1] *London County Council. Report of the County Medical Officer of Health and School Medical Officer for the year 1948.* London: Staples Press, Ltd. 2s. 6d.; by post, 2s. 10d.

School Health Services and Domiciliary Midwifery

The report embodies that of the school health service. Many more children have been subject to routine medical inspections. The number is smaller than pre-war, but, then, the school population is smaller. The number of children of school age in London is only half what it was twenty years ago. The general nutritional level appears to have improved. If the new classification of "good," "fair," and "poor" corresponds to the old classification of "excellent," "normal," and "subnormal" and "bad," the children of "poor" nutrition now number only 3.2% of those examined, compared with 6.6% with "subnormal" and "bad" nutrition in 1938.

Each year the County Medical Officer stresses one special aspect of the council's work—in this report domiciliary midwifery. The council's midwives presided over 10,000 domiciliary confinements in 1948, and about 8,500 were undertaken by hospital district and district nursing association midwives. Something like one-third of all the confinements in London are non-institutional.

Apart from twenty-five tables of statistics, this volume contains a vast amount of information concerning the general public health services of London for which Sir Allen Daley and his staff are responsible. It is mentioned that the first grade of staff transferred from the borough councils to be integrated with the council's medical staff was that of assistant medical officer; the transferred officers had their salaries brought up to the level of the medical officers in the council's school medical service. Specialization in maternity or in child welfare work has been encouraged, and efforts have been made to create a close liaison with the hospitals both as regards the teaching of medical students in council clinics and by attaching council medical officers for certain periods to the maternity or paediatric departments of hospitals.

CHANGES IN NOTIFICATIONS

POLIOMYELITIS AND ENCEPHALITIS

New regulations[1] which came into operation on January 1 make a number of changes in the notification of diseases of the central nervous system. Three new definitions are given which conform with the international standard classification of diseases brought into use on the same date. These changes will also have the effect of extending slightly the range of clinical conditions notifiable under "acute encephalitis" and "meningococcal infection."

Acute Poliomyelitis

The distinction formerly drawn between acute poliomyelitis and acute polio-encephalitis was not an easy one, and has never been adopted in other countries. In Sweden and in some parts of the United States it has long been the practice to report cases of acute poliomyelitis (including polio-encephalitis) as such but with one of two sub-headings. "Paralytic" includes cases with either transient or permanent paralysis. "Non-paralytic" includes cases in which there is no paralysis but where the diagnosis was made on clinical signs with or without examination of the cerebrospinal fluid.

Obviously in the latter group of cases the diagnosis is often uncertain, but, if patients who were not paralysed when first notified and admitted to hospital become paralysed later, the ordinary procedure for correction of the diagnosis previously notified should be applied by the hospital.

Acute Encephalitis

This replaces the former heading "encephalitis lethargica." It is very doubtful whether true encephalitis lethargica now occurs in this country, and under the new sub-heading "infective encephalitis" can be included cases of all forms of encephalitis, some of obscure aetiology, which are presumed to be of microbic or viral origin.

[1]The Public Health (Acute Poliomyelitis, Acute Encephalitis and Meningococcal Infection) Regulations, 1949.

The sub-heading "post-infectious" covers those forms of encephalitis which sometimes follow such well-defined infections as chicken-pox, measles, mumps, vaccinia, etc.

Meningococcal Infection

This heading will cover all cases of meningococcal meningitis formerly notified as "cerebrospinal fever." It will also allow the notification of cases of illness due to fulminant and other forms of meningococcal infection without an initial meningitis.

CYPRUS FREED FROM MALARIA

SUCCESSFUL CAMPAIGN

The Secretary of State for the Colonies, Mr. Arthur Creech Jones, M.P., addressed a press conference on January 9 at which he announced the successful conclusion of the three years' anopheles eradication campaign in Cyprus. He said that that day was a public holiday in Cyprus in celebration of the event. When the campaign started there were 18,000 cases of malaria annually in Cyprus, which has a population of 456,000 and an area of 3,500 square miles. It was said that 70% of village children had malarial parasites in their blood. The number of cases on the island was reduced to about 100 last year, none of them new infections. Infant mortality, largely due to malaria, had dropped during the last seven years from 180 per 1,000 live births to fewer than 70.

Mr. Creech Jones introduced Mr. Aziz, C.B.E., Chief Health Inspector of the island, and three Cypriots, members of the eradication team, which numbered 770 at the peak of the campaign. Mr. Aziz, who had originally studied under Sir Ronald Ross, was sent to Egypt in the early part of the war to study eradication methods there, and on his return introduced into Cyprus a system which depended mainly upon spraying and the use of D.D.T. The three anopheline species which had to be combated were *A. superpictus*, breeding in shallow collections of water exposed to full sunlight; *A. elutus*, breeding in marshy collections of water; and *A. bifurcatus*, breeding in heavily shaded water and in caves and wells.

The first of these vectors was attacked in 1946 over an area of 500 square miles in the region of the Karpas peninsula, and the attack was highly successful, whereupon the campaign was extended to the whole island and against all three carriers. The attack was made with insecticides and larvicides, usually 4% D.D.T. in gas or fuel oil. Gammexane smoke was used in buildings with high ceilings and in places difficult of access. The spraying was carried out with locally made or imported "flit guns," and all the work was checked repeatedly by special squads.

The campaign, which cost under £300,000, or about 13s. per head of population, was financed by the Government of Cyprus, apart from an initial grant of £17,000 from the Colonial Development and Welfare Fund. Cyprus can now be declared free of malaria-carrying mosquitoes, and a constant watch is maintained against reintroduction by ships or aircraft. Mr. Creech Jones paid a tribute to the great part played in the work by Dr. H. M. Shelley, Medical Officer of Health of the island. Mr. Aziz, the Executive Officer of the campaign, and Mr. Veysi, Inspector in the Medical and Health Department. He added that this was only one—although up to the present the most brilliantly successful—of the instances of similar work under the auspices of Colonial Governments. He referred to the work which is being done in British Guiana (Georgetown), Sierra Leone, and Mauritius. "We are not very forthcoming in announcing some of the victories gained on the social and economic fields of our Empire, but all along the line signal victories are being won."

A message of congratulation from the Colonial Secretary to the Governor of Cyprus, Sir Andrew Wright, stated: "Mr. Aziz and his loyal team, who have spent so many arduous hours patrolling and re-patrolling plains, marshes, and mountains in pursuit of their prey—a work all the more laborious in these last stages when there were no more mosquitoes to be found—have won fame among doctors and scientists all over the world

and have set an example which other countries are already making haste to follow."

During Lord Winster's governorship a bet was made between him and the High Commissioner of Sardinia, where a similar eradication campaign is being waged, on which island should first declare itself free of the malaria-carrying mosquito. Cyprus has won the bet, and 100 litres of Sardinian wine is on its way to Nicosia to be distributed among the men of the eradication service.

ORDER OF ST. JOHN OF JERUSALEM

The *London Gazette* has announced the following promotions in, and appointments to, the Venerable Order of the Hospital of St. John of Jerusalem:

As Knight: Colonel J. L. Hamilton, M.C., T.D., M.D. *As Commanders (Brothers):* The Hon. Paul Boffa, O.B.E., M.D., Lieutenant-Colonel W. George, *M.C.*, T.D., M.B., Drs. H. E. Skeete, O.B.E., F. R. B. H. Kennedy, M.B.E., James Lamberton, E. H. Shaw, O. T. J. C. de H. Clayre, F. H. Edwards, W. F. J. Whitley and A. P. Spark. *As Associate Commander (Brother):* Dr. G. Haridas. *As Officers (Brothers):* Brigadier A. L. Dawkins, O.B.E., M.B., F.R.C.S., Major A. R. Home, M.B., Drs. C. P. Craggs, J. G. Baldacchino, J. M. Cruickshank, A. D. Macdonald, P. Grima, F. L. Firkin, B. S. Collings, R. H. O. Garbutt, A. J. Owston, and E. H. Capel. *As Associate Officers (Brothers):* Drs. Chen Su Lan, K. Vellasamy, B. C. Cohen, and M. C. Vayma. *As Serving Brothers:* Lieutenant-Colonel F. K. Mugford, M.B., Major D. H. Beatson, M.B., Mr. B. G. Scholefield, F.R.C.S., Drs. H. W. Round, D. T. Richards, H. E. Martin, J. E. King, E. B. Garrett, W. S. Dixon, C. L. Worthington, G. Gillies, J. S. Taylor, R. Meyerstein, P. H. Boshoff, S. C. Hattingh, W. H. Cruickshank, R. Muscat, T. J. Agius-Ferrante, J. Moffat, C. C. Fleck, A. H. Williams, P. W. Mitchell, C. C. Jungfer, T. James, J. McAleer, and Hotin Lee. *As Associate Serving Brother:* Dr. Ramashwar Singh.

NATIONAL FORMULARY, 1949

AMENDMENTS

The Joint Formulary Committee has decided that where preparations appear in the *National Formulary, 1949,* and the *British Pharmaceutical Codex, 1949,* under the same main title or synonym, they shall, with the exception of guttae cocainae and tabellae ferri sulphatis compositae, be dispensed or prepared according to the formula of the *B.P.C.* This will apply from the date on which the Minister of Health decides that the *British Pharmaceutical Codex, 1949,* shall replace the *British Pharmaceutical Codex, 1934,* for National Health Service purposes.

The following list gives those preparations of the *National Formulary* chiefly affected by this decision. Where the main titles are not identical, that of the corresponding *B.P.C.* preparation is given in parentheses.

Applicatio dicophani.
Collodium acidi salicylici.
Collyrium acidi borici.
Collyrium acidi citrici.
Collyrium boracis compositum.
Collyrium hydrargyri oxycyanidi
Collyrium sodii bicarbonatis.
Collyrium sodii chloridi.
Collyrium zinci compositum.
Conspersus acidi salicylici compositus.
Conspersus hydrargyri subchloridi compositus.
Conspersus talci boricus (Conspersus talci borici, *B.P.C.*).
Conspersus zinci oxidi et amyli compositus.
Cremor calaminae compositus.
Cremor proflavinae.
Cremor zinci (Cremor zinci oxidi, *B.P.C.*).
Cremor zinci et ichthammolis (Cremor zinci oxidi et ichthammolis, *B.P.C.*).
Gargarisma phenolis.
Gargarisma potassii chloratis et phenolis
Guttae aethylmorphinae.
Guttae argentoproteini.
Guttae argentoproteini mitis.
Guttae atropinae sulphatis.
Guttae cocainae et homatropinae.
Guttae cupri sulphatis.
Guttae fluoresceini.
Guttae homatropinae.
Guttae hyoscinae.
Guttae lachesinae.
Guttae penicillini.
Guttae physostigminae
Guttae pilocarpinae.
Guttae proflavinae.
Guttae zinci sulphatis.
Injectio sulphadimidinae sodii
Insufflatio argenti picratis.
Liquor boracis et formaldehydi.
Liquor iodi simplex.
Lotio calaminae oleosa.
Lotio cupro-zincica (Lotio cupri et zinci sulphatum, *B.P.C.*)
Lotio picis carbonis et plumbi.
Lotio plumbi.
Lotio plumbi et glycerini.
Lotio plumbi evaporans.
Mistura ammoniae et ipecacuanhae composita
Mistura ammonii chloridi et morphinae.
Mistura cascarae.
Mistura ferri et ammonii citratis.
Mistura ipecacuanhae alkalina.
Mistura potassii bromidi.
Mistura potassii bromidi et valerianae.
Mistura potassii iodidi ammoniata.
Mistura rhei ammoniata cum soda.
Pasta picis carbonis.
Pasta resorcinolis (Pasta resorcinolis composita, *B.P.C.*).
Pasta resorcinolis mitis (Pasta resorcinolis composita mitis *B.P.C.*).
Pasta zinci oxidi cum acido salicylico.
Pigmentum iodi compositum.
Pigmentum iodoformi compositum.
Pigmentum podophylli.
Pigmentum tinctorium.
Tabellae ferri carbonatis.
Troschisci ammonii chloridi.
Troschisci formaldehydi.
Unguentum acidi benzoici compositum
Unguentum acidi borici flavum.
Unguentum acidi salicylici et sulphuris
Unguentum cinchocainae compositum.
Unguentum dithranolis forte.
Unguentum hydrargyri ammoniati et picis carbonis
Unguentum ichthammolis.
Unguentum iodi denigrescens.
Unguentum iodi denigrescens cum methylis salicylate
Mistura acidi acetylsalicylici pro infantibus.
Mistura ipecacuanhae ammoniata pro infantibus.
Mistura stramonii et potassii iodidi pro infantibus.

Reports of Societies

CARDIO-OESOPHAGEAL OBSTRUCTION

At a meeting of the Liverpool Medical Institution on December 15, 1949, Mr. F. RONALD EDWARDS read a paper on "Cardio-oesophageal Obstruction"; the president, Professor CHARLES WELLS, was in the chair.

Mr. EDWARDS discussed the more common causes of obstruction at the cardio-oesophageal junction: cardiospasm, peptic ulceration and stricture formation, and malignant disease. The salient feature was dysphagia. It started as a definite pain due to excessive peristalsis, but as soon as the circular muscle fibres weakened dilatation took place, and the pain was replaced by a sensation of distension. In cases of long-standing obstruction the oesophagus might become a functionless sac. Hypersalivation and regurgitation were common, but vomiting of the gastric contents was usually impossible. The calorie value of the diet progressively diminished as it became more fluid, and ultimately there was a hypo-proteinaemia which might be very difficult to correct and which increased the risks of surgery.

In cases of cardiospasm, the oesophagus acted as a "drip-feed" and loss of weight might be delayed to a late stage; the unfortunate patient spent a large part of his life eating, with

serious economic and social complications. Peptic ulceration of the oesophagus was due to functional incompetence of the cardiac sphincter, associated with widening of the oesophago-gastric angle, secondary to hiatus herniation. A wide hiatus was present in a small proportion of individuals because of late descent of the stomach in the embryo stage. A true congenital short oesophagus was present in only about 5% of cases. The para-oesophageal hernia without shortening of the oesophagus did not produce peptic ulceration. Secondary stricture formation occurred if hyperchlorhydria was present; associated juxtapyloric ulcers were common in these cases.

Methods of Treatment

An area extending for 5 millimetres on each side of the oesophago-gastric mucosal junction was very prone to malignant disease, with adenocarcinoma more common than the squamous cell variety. Three cases of adenocarcinoma were described. A study of the lymphatic drainage of this area was important and in all cases the glands around the coeliac axis were involved early. It was necessary to remove the lesser omentum, greater omentum, coeliac nodes, mediastinal nodes, and supra-pancreatic nodes. For adenocarcinoma total gastrectomy should be undertaken and the lower end of the oesophagus, two-thirds of the pancreas, the spleen, and the related lymph nodes should be removed in continuity, and an oesophago-jejunal anastomosis performed. For a squamous-cell carcinoma a subtotal gastrectomy might be performed and oesophago-gastric anastomosis completed the operation; but here again an extensive resection of the lymph nodes was required.

Cardiospasm should be treated by Heller's operation of oesophago-cardio-myotomy if simple measures failed, and the operation should be undertaken early, preferably through the abdomen. The incision down to the mucosa should be at least 2 inches (5 cm.) long. Other operations were not recommended. The speaker described 15 cases in which Heller's operation had been undertaken with uniform success.

The treatment of well-established peptic ulceration of the oesophagus was difficult. Repeated dilatations, the administration of alkalis, and sleeping in the erect position would all help. If the condition was found early, restoration of the normal anatomy might produce cure. Excision of the stricture with oesophago-gastric anastomosis after a two-thirds resection of the stomach had been recommended, but experience of this procedure was not yet sufficient to allow of its evaluation.

A plea was made for the more extensive application of radical operation in all cases of carcinoma of the stomach, in view of the poor long-term results with any other form of treatment. The post-operative course might be difficult because of hypoproteinaemia and vitamin deficiency, and great care must be taken to restore these deficiencies so far as possible pre-operatively. In 21 cases of oesophago-gastric resection there had been two post-operative deaths: one from bronchopneumonia three days after operation, and one from hypoproteinaemia nine weeks afterwards. The patients tolerated these operations very well and four of them were over 70 years of age. The follow-up showed seven patients dead, including the two post-operative deaths; the most usual cause of death was metastases in the 40–50 age group. The older men and women did well. It was realized that the follow-up was not yet long enough for any definite conclusions to be drawn. However, four patients survived out of the five followed for two years since operation.

The paper was illustrated with a colour film of oesophago-gastrectomy for a squamous-cell carcinoma of the lower end of the oesophagus.

The Ministry of Fuel and Power has changed a number of titles of officers in its Mines Inspectorate. The Chief Mines Medical Officer is renamed Principal Medical Inspector of Mines; the Deputy Chief Mines Medical Officer becomes Deputy Principal Medical Inspector of Mines; and the Mines Medical Officer becomes the Medical Inspector of Mines.

Correspondence

Fifty Years of Medicine

SIR,—Perhaps a word of congratulation on your first 1950 number from an old contributor to the *Journal* will not come amiss. I think the marshalling of the series of retrospective articles is really an editorial triumph and deserves the profession's gratitude. To my mind it gives us all that vision of medicine as above all political wrangles of which we have been in need, and effectively recalls to us the foundations of our self-respect. I can stretch my imagination to think how it is warming the heart of my one-time friend Dawson Williams.—I am, etc.,

Woolstone, Berks. K. W. MONSARRAT.

SIR,—As a member of the B.M.A. for over 25 years I feel proud to express to you, Sir, and to the editorial staff my heartfelt congratulations on the praiseworthy effort in presenting to your readers this remarkable number of the *Journal*—Fifty Years of Medicine. It is, indeed, a noble and distinguished account of a noble and distinguished achievement.—I am, etc.,

London, S.W.5. J. M. RAPHAEL.

SIR,—I think the Editor, contributors, and staff of the *British Medical Journal* are to be congratulated for publishing one of the most interesting and informative issues, Fifty Years of Medicine. One marvels at all the advances in preventive medicine, treatment, and aids to diagnosis that have been made in the past fifty years, and one is rather apt to take all these for granted, without paying due respect and gratitude to the pioneers who have done so much to help us. We are certainly under a great obligation to them, and should avoid over-indulgence in these benefits. At the same time one regrets the gradual passing of that great man "the general practitioner"—guide, philosopher, and friend of his patient. He, not being a specialist, could clearly see the wood for the trees and take an unbiased view of his patient's case.

Admiration is due to the older generation who, equipped only with their five senses and a stethoscope, were correctly able to diagnose a large proportion of their cases. I wonder how the younger generation would fare under similar circumstances if they suddenly found themselves bereft of all modern aids to diagnosis. I think it would take many years to redevelop the "sixth" or "clinical diagnostic" sense; it seems a great pity that this should be lost.—I am, etc.,

Burnham-on-Sea, Somerset. CEDRIC C. MECREDY.

SIR,—In your leading article on "The Relief of Pain" (January 7, p. 64) a statement is made for which I fear I may be ultimately responsible, that "the procedure of injecting the nerve trunks at their exits from the skull (for the relief of trigeminal neuralgia) was first advocated by Pitres and Verger in 1902 and Schloesser in 1903." I made this statement in my book *Neuritis and Neuralgia* in 1926 (p. 175), but I corrected it in my subsequent book *Facial Neuralgias* in 1937 (p. 33).

Abadie and Verger, working in Pitres's clinic, used cocaine in 20% solution, injected beneath the skin of the area of pain reference, followed three or four days later by 1 ml. of 45% or 60% alcohol, in December, 1901, and January, 1902, publishing their results in the *Bulletins et Mémoires de la Société de Médecine et de Chirurgie de Bordeaux*, 1902 (pp. 59 and 91). This volume is not in the library of the Royal Society of Medicine but can be seen in the library of the Royal College of Surgeons. The credit, therefore, of being the first to use alcohol injections to the trigeminal nerve branches at their deep foramina of exit from the skull belongs to Schloesser alone (*Zeitschrift für Augenheilkunde*, 1903, **10**, 335). He used the intra-oral route for injection through the soft palate, which was superseded in 1906 by Levy and Baudouin's lateral route through the sigmoid notch.—I am, etc.,

London, N.W.1. WILFRED HARRIS.

Cancer Statistics

SIR,—Now that many regional hospital boards are busy organizing a cancer service, siting their radiotherapy centres and, it is hoped, organizing the surgical treatment of cancer, it is perhaps opportune to discuss the subject of cancer statistics. At least one organization is working out how statistics should be presented and evaluated, all of which is very essential. In designing a house it is valuable to know what the roof will look like, but it is equally important to have a proper foundation which is to support the house and roof. At present there is no foundation.

The foundations of cancer statistics are the clinical records made at the bedside by the clinicians in charge of the case and the surgeon who operates. Those of us who have an opportunity to read such records realize that they only refer to certain positive points which may be of importance for that particular patient, and rarely if ever is a thought given to what may be important for cancer statistics. The teaching hospitals try to teach students to take notes, but there seems to be a prejudice against the use of case sheets with headings to remind the student of what points he should describe and which will be of value for statistics. Statistics can only answer questions that are asked, and these questions must be formulated three to five years before the answers can be given. Surely, therefore, it is urgent that a committee with representatives of regional boards should be set up to go into the problem.—I am, etc.,

London, W.1. MALCOLM DONALDSON.

Silico-tuberculosis

SIR,—Dr. C. M. Fletcher, who has himself done such excellent research into pneumoconiosis, in his letter (December 10, 1949, p. 1351) raises certain points of criticism about our paper (November 19, p. 1148) on mortality and survival rates in males with silicosis and silico-tuberculosis, to which we would like to reply. The method of tabulation and analysis of the data is, we feel, clearly stated in the paper and the conclusion drawn by Dr. Fletcher in his first paragraph is erroneous. The conclusion to be drawn is that, of the workers in the trades under consideration who were suffering from silicosis and who were alive at the age of 40 and who at some time developed tuberculosis, half will be alive and half will be dead by the age of 58.

The method of presentation of survivorship is not ideal. The ideal method of limiting the experience to the period between the age of onset and death is not practical with our data, since the age of onset cannot be established with any certainty either in the case of those men who develop silicosis or among those who subsequently contract tuberculosis. Moreover, the experience of the 189 men who were still alive would have been lost and the results would have been biased by including, proportionately, too many with a very short survival time.

The diagnosis of silicosis during life was made on radiological appearances together with a degree of occupation risk. The diagnosis of tuberculosis was a clinical diagnosis. The proportion of sputum-positive cases among those still alive is 53%. The proportion of all cases of silico-tuberculosis with a recorded positive sputum is about 80%. There is frequently a considerable time lag between diagnosable tuberculosis in a case of silicosis and the obtaining of a positive sputum by the smear method. This is shown by the following examples:

1. Stone mason, aged 52, diagnosed silicosis and pleural effusion; T.B. negative. Aged 63, silicosis and pulmonary tuberculosis; T.B. positive. Aged 64, died of silico-tuberculosis.
2. Grinder, aged 50, diagnosed silicosis and pulmonary tuberculosis; T.B. negative. Aged 55, sputum found T.B. positive. Aged 57, died of pulmonary tuberculosis and silicosis.

As one does not wait for a positive sputum to diagnose and treat pulmonary tuberculosis in other patients it would be irrational to wait for a positive sputum before diagnosing and treating pulmonary tuberculosis in a man with silicosis. We recognize that there are certain special features in the pneumoconiosis which occurs in miners in the South Wales coalfields. In the South Yorkshire coalfield silicosis is mainly a risk to the men who deal with the rock, such as rippers and drifters. Our observations, therefore, may not be applicable to coal-miners in other coalfields.

We apologize to Dr. Fletcher if by our quotations from his paper we have misrepresented his views. The quotation is correct, but it may have been taken out of its context.—We are, etc.,

H. MIDGLEY TURNER.
W. J. MARTIN.

Fate of the Foreskin

SIR,—Dr. Douglas Gairdner's article (December 24, 1949, p. 1433) gives us most useful ammunition for the occasions when one has to discourage a suggestion that circumcision be done on a boy. He quotes Higgins's opinion that circumcision should not be considered until after the age of, say, 2 or 3 years. I wish to add a plea that circumcision should be avoided at this age. We are realizing that children admitted to hospital may take a logical (if false) conclusion that their parents do not want them any more, and, if an operation on an organ so important to him follows, the idea that he is being punished is even more likely to arise. Furthermore, we are taught that the boy is at this age in rivalry with his father for possession of his mother, and it seems very possible that the development of his conscience and his sexual outlook might be disturbed.

Even if it is necessary, circumcision should if possible be postponed once the child is several months old to an age at which the purpose can be understood and will not be misunderstood by the boy. Could Dr. Gairdner say what is the mortality of circumcision done in the first month of life and over the age of, say, 5 years?

The other point which I would make is to ask for a better critical examination of what Dr. Gairdner rather unfairly describes as "minor advantages of circumcision." Most people are fairly satisfied with themselves as they are, but of the three married adult males consulted in the last two days I found all three were unshorn and two wished they had been. I do not think that "the erotic superiority of the shorn member" is disproved or established by the excessively brief critical examination given in the article, and I would ask that Dr. Gairdner extend his excellent review of the physical aspects of circumcision. The proportion of wives who get no emotional satisfaction from coitus is perhaps four out of five. This may well be that too many men are too egotistical in their technique, but, while there is "more to marriage than four legs in a bed," it seems possible that by delaying the man's and increasing the chance of the wife's response circumcision may perhaps contribute to happy marriages. I do not know the answer, but I would like to, and I hope that Dr. Gairdner will put us further in his debt by reviewing at least some of these other aspects.—I am, etc.,

London, S.E.1. R. C. MACKEITH.

SIR,—I have read with appreciation the valuable article by Dr. Douglas Gairdner (December 24, 1949, p. 1433) and also your leading article (p. 1458). I quite agree that one of the arguments against the operation is that possible injuries may be caused by it, even though some of these ought never to occur. I well remember, when doing infant-welfare work, a mother asking me to examine her recently circumcised baby. I found that the glans penis had been completely amputated. The operator had evidently, after drawing the prepuce forward, cut behind the glans instead of in front of it. I have been told that the N.H.S. Act has "killed," or at least largely reduced, routine circumcision. If so, that is one good mark for the Act.—I am, etc.,

Leicester C. KILLICK MILLARD.

SIR,—With all due deference I should like to question some of the conclusions reached in Dr. Douglas Gairdner's most illuminating article on "The Fate of the Foreskin"

(December 24, 1949, p. 1433). He makes the following statements. "About 16 deaths in children under 5 years occur each year from circumcision." "A conservative estimate of 20%" of all males born are circumcised. "Deaths from penile cancer number about 150 a year" (i.e., in the uncircumcised 80%). "Circumcision in the first five years of life protects absolutely from penile cancer." These would appear to indicate that about 187 cases of fatal penile cancer would be prevented annually for the potential loss of 80 lives (but see next paragraph) if all male children were circumcised within the first five years of life.

It is inferred that the sixteen deaths a year attributable to circumcision are mainly anaesthetic deaths and not due to the actual operation. Two points emerge from this: first, that if the child were circumcised early enough an anaesthetic would not be required; and secondly, it is possible that some of these children succumbed because of their status lymphaticus—which would have proved just as fatal in later life when they would have been subjected to anaesthesia for tonsils and adenoids or the commoner surgical emergencies.

A child who had his interest centred on his prepuce and glans penis at such an early stage in his life, as suggested by Dr. Gairdner, would almost certainly be more prone to the neurotic upsets associated with sex than one who had no subprepucial space to clean or be kept clean. Being taught to clean one's own ears out is probably psychologically innocuous, but pseudo-masturbatory lessons would surely give rise to alarm in our psychiatric colleagues.

If Dr. Gairdner's suggestions about cleaning the subprepucial space were followed the incidence of paraphimosis, etc., in young children would probably increase, due to the attempts of overzealous mothers to reach the stage of full retractability at the earliest possible moment. Early circumcision would prevent this. It is one thing to advise a mother that her infant's glans will see the light of day spontaneously if she waits long enough, but definitely another thing to prevent her from accelerating the process by domestic (as opposed to surgical) manipulations.

If penile carcinoma is really the result of the combination of a low intelligence, a low standard of personal hygiene, and the presence of the prepuce after the age of 5, then the obvious answer is to remove the foreskin, since the other two are almost totally resistant to therapy. A person of meagre intellect and consequently of dirty habit is not the right type to deal adequately, if at all, with the retained smegma under his foreskin.

Finally, should the resident medical officers of our hospitals bring the charge that they have neither the facilities nor the time to circumcise five times the number of infants they are already doing, my answer would be that the general practitioner is qualified to perform this short operation.—I am, etc.,

Plymouth. B. J. PECK.

SIR,—Dr. Douglas Gairdner (December 24, 1949, p. 1455) convincingly shows how very few are the medical reasons for circumcision of infants. To account for the increase of the practice a hygienic explanation is often given. This is an ancient aetiological myth or a rationalization of a process which has a very different source. No doubt the growth of the myth has something to do with the astonishing advances and increased prestige of surgery seen, for example, in the onslaughts on numberless juvenile tonsils, so that many a parent feels negligent if her child is not exposed to one or both of these procedures.

But the meaning of this most ancient and world-wide custom, in spite of all the speculations to which it has given rise, is surely of a religious nature. In your leading article (p. 1458), under the significant title "A Ritual Operation," you say, "At its inception the practice seems to have had an essentially religious connotation." I think this an understatement. My own belief is that always the underlying motif, often unconscious, has been of this kind.

Sacrifice has a prominent place in comparative religion. In the past it has sometimes appeared as murder or, what is much the same, self-destruction, but in spite of the "atomic age" in which we live both are repugnant to the normal man. Generally reward in this world or the next is expected, and the greater the sacrifice the greater the reward. Lavish philanthropy leaps to the mind as an illustration, but surely the greatest offering that can be made is that of one's immortality or, what is another facet of the same thing, one's power of reproduction. And here the fairy reasoning of "make believe" takes sway: there is no need to offer the phallus, for its foreskin may be substituted. Dr. Gairdner records an arresting reply to his question to a parent why she wanted her infant to be circumcised. There was no talk of health, but simply, "We believe in it."—I am, etc.,

London, S.W.1. E. GALLOP.

Infantile Gastro-enteritis Contracted in Hospitals

SIR,—Study of the article by Drs. K. B. Rogers, S. J. Koegler, and John Gerrard entitled "Chloramphenicol in the Treatment of Infantile Gastro-enteritis" (December 31, 1949, p. 1501) reveals that cross-infection in children's hospitals is still present to what, I submit, must be considered an alarming degree. In the case of infants under 12 months, has not the time come when under the National Health Service a new effort should be made to afford to the child in its own home the highly skilled treatment the first-class hospital offers, fuller advantage being taken of the services of general practitioners, district nurses, and health visitors?

The work of hospital out-patient departments could be greatly extended for cases where hospital supervision is essential. Babies, unlike sick adults, are easily transported to hospital, and there they need only leave the shelter and safety of their mothers' arms for the short period of necessary examination and treatment. A recent bitter experience of having to notify a leading hospital that a 4-months old baby, admitted in good health for operative treatment and detained ten days, had died two days after discharge as a result of a severe attack of gastro-enteritis which was obviously present when the child was handed over to the mother, prompts me to write this plea for less hospitalization.

With better medical co-operation could not many young infants under 12 months now being admitted to hospital be treated with efficiency and with greater safety outside the hospital wards? The list of cases admitted for treatment in the article referred to makes significant reading. It includes as "reason for admission" marasmus at 1 month, marasmus at 2 months, otitis media at 2 months, prematurity at 3 months, pseudoparalysis due to congenital syphilis at 3 months, thrush and parotitis at 4 months, and pink disease at 8 months. Prevention even in these days of wonder drugs is still better than cure.—I am, etc.,

Nailsworth, Gloucestershire. MARGARET N. DUNSTAN.

Reactions to Bee- and Wasp-stings

SIR,—An anaphylactoid response to a bee-sting in a patient who had previously been stung by a wasp, as described by Surgeon Commander W. R. S. Panckridge and Surgeon Lieutenant C. Q. Henriques (December 10, 1949, p. 1354), has been previously reported, while a bee-sting sensitizing to a subsequent wasp-sting has also been described.[1] It has been postulated[2] that a reaction following a bee-sting could be caused by: (*a*) some toxic effect of the venom which causes tissue injury and histamine liberation; (*b*) an allergic reaction in pollen-sensitive patients due to the pollen adhering to the bee; and (*c*) allergic reactions due to sensitization to bee protein.

Almost certainly the lancet of the bee is free from contamination by pollen. Moreover, in nine bee-sensitive patients seen in 1949 I have only twice found the patient sensitive to grass pollen. The pollen adhering to the bee would not be from the grasses, which are wind-pollinated, but would depend upon the flower the bee had been visiting. It is found by skin tests that bee-sensitive patients are sensitive to extracts of bee-stings, to bodies with stings removed, and to whole bee. An overdose of a watery extract of drones has caused a reaction in a sensitive patient which is quite indistinguishable from that of a bee-sting. There seems, therefore, no necessity to explain the severe and

sometimes fatal reaction after a bee-sting as due to the presence, among other things, of hyaluronidase, as suggested by Dr. J. Pepys (December 24, p. 1474). A timothy-grass-pollen extract acting as a dominant group antigen for all the grasses will hyposensitize other grass-pollen sensitivities. In the same way it should be possible to hyposensitize with a wasp extract a bee-sting-sensitive individual. "Desensitization" to a bee or wasp sensitivity is possible but it is not easy, as local or general reactions may occur. In my experience the antihistaminics, while useful when applied as a cream to allay a mild local irritation, do not influence a general reaction when taken by mouth. Self-administered adrenaline still remains the treatment of choice because of the speed of onset of the severe symptoms. —I am, etc.,

London, W.2. A. W. FRANKLAND.

REFERENCES

[1] Prince, H. E., and Secrest, P. G., *J. Allergy*, 1939, **10**, 379.
[2] Benson, R. L., and Semenov, H., ibid., 1930, **1**, 105.

SIR,—Though I cannot solve the problems presented by Surgeon Commander W. R. S. Panckridge and Surgeon Lieutenant C. Q. Henriques on the treatment of wasp and bee-stings (December 10, p. 1354), I feel that my personal experiences as a bee-keeper for more than twenty years may be of interest to them.

Early in my bee-keeping career I found that gloves (strong enough to be protective) were a cumbersome nuisance and I soon discarded them. As a rule I collect some two or three dozen stings during the season. After the initial stab there is some aching pain for a minute or two followed by a rapidly developing local oedema. This continues for about 24 hours, subsiding during the next 12 hours, when it is accompanied by itching. I think the pain becomes less noticeable with each succeeding sting of a series. Stings near the ends of the fingers are more painful than those where the subcutaneous tissues are lax and the swelling is unconfined.

I remove the stings in the approved manner as soon as convenient, but I have never applied any of the traditional remedies, as it seems to me improbable that anything could pass through the minute puncture to neutralize the toxin. I have occasionally suffered mass attacks, when my hands and wrists were covered with struggling bees anchored by their stings, and on at least one of these occasions there has been some dyspnoea and palpitation, though I am not sure that these constitutional symptoms might not have followed any other comparable painful and alarming experience.

As a rule, my reaction to stings is one of annoyance that I have angered the bees (either through my clumsiness or the choice of an unsuitable day for manipulation) so much that they immolate themselves in defence of the colony. Perhaps this feeling of annoyance is sufficient to liberate enough adrenaline to counteract the constitutional effect of the venom. To be able to supplement this mechanism in case of need it would seem desirable, as your correspondents suggest, for the bee-keeper to add a hypodermic syringe and a bottle of adrenaline solution to his bag of tools.—I am, etc.,

Pickering, Yorks. HAROLD UPCOTT.

Parturition and Pneumonectomy

SIR,—The object of joining in this correspondence (October 1, p. 758, and December 17, 1949, p. 1414) is to state that the majority of patients after pneumonectomy can return to, and in some cases start for the first time, a normal life. A normal life for a man may involve manual labour and for a woman certainly includes child-bearing. It is now over fifteen years since pneumonectomy became an accepted procedure for suppurative disease and neoplasia, hence there can be no doubt of the immediate results. A typical case is as follows:

The patient was aged 17 when in July, 1940, she underwent left pneumonectomy for saccular bronchiectasis. On August 19, 1940, she was discharged from hospital—condition satisfactory. From 1941–4 she was in domestic service and well for more than six consecutive months for the first time in her life. In 1944 she married a miner. On May 7, 1945, she was delivered of a full-term male child. On November 3, 1947, she underwent appendicectomy for gangrenous appendicitis. On June 17, 1949, she was delivered of a full-term female child. My obstetric colleague Dr. W. J. Clancy had no difficulty in the pregnancies or the confinements. None was expected.

—I am, etc.,

Sheffield. JUDSON T. CHESTERMAN.

Haematemesis Due to "Disprin"

SIR,—Haematemesis has often been noted as being due directly to the taking of salicylates by mouth. "Disprin," a form of aspirin fairly recently put on the market, was thought to be, and probably is, relatively innocuous to the gastric mucosa. This may be by virtue of the calcium carbonate incorporated in the tablet. Nevertheless, in the following case the haematemesis which occurred seems to have been due directly to the taking of the tablets.

A man aged 46 years had "muscular rheumatism" for a few days before his admission to the hospital. For this he was taking disprin tablets, one every four hours. He complained of a sharp burning, epigastric pain shortly after taking each tablet. He took 24 tablets in all. Five days before his admission he felt sick, and vomited a considerable amount of blood. Since then he had been passing blood per rectum and his motions became black and tarry. This persisted, and he felt very weak and dizzy. There was no past history whatsoever of stomach trouble, and he was a man who had always had an aversion to taking tablets of any sort. In fact, he stated that he had never had an aspirin in his life to his knowledge.

When he was admitted, he was very pale and had obviously lost a considerable amount of blood. There was some tenderness in his epigastrium, but no other abnormality was found in any system. His condition was such that we felt an urgent transfusion was indicated and he was therefore given two pints (1.1 litres) of blood. Morphine ¼ gr. (16 mg.) was given at this time. From then he made an uneventful recovery. He was fully investigated to exclude any blood dyscrasia and everything appeared to be normal. His faeces were found to contain blood for some time after his original haematemesis. He was quite well when discharged home and returned at a later date to the out-patient department, when he had a barium meal. This failed to show any abnormality. We have seen the man several times since the above episode and he has remained quite fit and well. He is not troubled with any indigestion.

Though it may appear that the evidence is not conclusive that the haematemesis was, in fact, due to disprin, we feel that it is at least very suggestive.

We would like to thank Dr. L. Glick, under whose care the patient was admitted, for his help and advice in this case.

—We are, etc.,

CYRIL JOSEPHS.
Dewsbury. SHANTI NARAIN MATHUR.

Chilblains

SIR,—Dr. H. S. Russell (December 24, 1949, p. 1473) inquires. "Has anyone ever been cured (of chilblains) by taking calcium?" Following an enforced change to a life of less physical activity some fifteen years ago, I became a sufferer from this most distressing complaint. After suffering severe discomfort during frosty weather for some years and finding all reputed remedies quite ineffective I resorted to the subcutaneous injection on alternate days of 1 ml. of colloidal calcium with vitamin D. Following the third injection relief was complete, and symptoms did not occur for several months. Every year since I have undergone this treatment at the first onset of symptoms. Sometimes I find it necessary to have one or two more injections before the winter ends: sometimes one course suffices.

As I am not engaged in the practice of clinical medicine I have no long series of cases to report, but I have similarly treated about a dozen members of my family, domestic staff, etc., with equally successful results in every case. I have consequently been surprised to see so few references to this method of treatment in the relevant literature and have sometimes wondered whether the complete success in my short series of cases was no more than a coincidence. Nevertheless it seems to

show at least that a proportion of cases does yield to this treatment. It does not, however, provide an answer to Dr. Russell's question, for I believe that the concentration of calcium in the preparation used is only 0.5%, and it may be that the 5,000 i.u. of vitamin D is of more therapeutic value.

My excuse for recounting this personal experience is the very real suffering, both physical and mental, still experienced by so many as a result of what is frequently regarded as a childish and even risible complaint. I have recently seen somewhat casual references to the successful use of similar methods of treatment, and there seems to be sufficient favourable evidence to justify a controlled investigation of a large number of cases. —I am, etc.,

London, E.C.1. E. F. W. MACKENZIE.

SIR,—I was very interested to read Dr. Henry S. Russell's letter (December 24, 1949, p. 1473) and to note his explanation of the aetiology of chilblains. I came to a very similar conclusion myself, and quote the following extract from an article that I wrote in the *British Medical Journal* of February 21, 1948 (p. 336):

"Exposure to cold causes a vasoconstriction of the subcutaneous arteries and interference with cellular metabolism resulting in the formation of irritating metabolites. On warming the part, if the arterial spasm relaxes the metabolites are removed and no lesion supervenes. If, however, the arterial spasm does not relax within a reasonable time more metabolites are formed at the site because of the increase in cellular metabolism due to warming the part; this causes irritation, oedema of the corium, and thus interference with venous drainage, setting up a vicious circle and producing a chilblain. Thus a chilblain will result only when cold causes arterial spasm and there is an upset of the balance between vital cellular activity and venous drainage. It is claimed that this theory explains the many and varied anomalies of chilblain production."

As regards treatment, I have found nicotinic acid in 50-mg. doses taken three times daily immediately after food to be the most generally effective method of relieving the pain and irritation of chilblains.—I am, etc.,

Oxford. R. J. GOURLAY.

Authors and Psychopaths

SIR,—I would like to congratulate Dr. W. Russell Brain (December 24, 1949, p. 1427) and the writer of your leading article (p. 1457) on their fascinating contributions to thought and literature, and I am convinced that we should pursue further the question whether human thought has been and still is being guided not by sane men but by psychopaths. Unfortunately there is, in analysing medical history, a great difficulty, and that is the unreliability of the data available. For example, the popular story that Henry VIII died of taboparesis and gummatosis cannot be proved to-day; in fact there is a formidable differential diagnosis—also that unfortunate monarch has no opportunity to clear himself. Recently I read an account of the post mortem on Byron, which supposedly proved that he died of alcoholic uraemia; but to me the pathological findings described by the author suggested more strongly cerebral malaria. Who can prove either theory? Often the evidence quoted is that of an enemy or biased for some other reason. How much more difficult is a mental diagnosis of a dead man. But how tempting to jump to conclusions.

Miss Reynolds's description of Johnson's gestures is emotional and sensational, and only that of the observant lawyer gives us reliable clinical information (see *Life of Johnson*, year 1764). Boswell's differential diagnosis between chorea and habit spasm (see year 1739) is a masterpiece, although he refrains with legal caution from committing himself. Also his proof that Johnson was not psychotic is convincing (see year 1729). Undoubtedly Johnson was "maladjusted." The human race is preserved in sanity and stability by a natural but unjustified sense of optimism, which is likely to disappear when the subject engages in deep and serious thought. To reconcile life with pain and evil is impossible for most thinkers, but fortunately the vast majority of the population prefer not to think, and so society continues to tolerate this most illogical existence. Had not Johnson good reason for his odd behaviour? Is it not possible that Swift's means of self expression to Stella was in some way superior to that between ordinary men and women? Was Dickens really a sadist, and are detective-story writers potential mass murderers? After all, writers and poets must please their public in order to live, so is it not possible that the latter, whose natures they have divined, are the real sado-masochists and criminals at heart?

I trust that these defenceless men will not be tried solely by psychiatric standards. The psycho-analyst must surely be to some extent the enemy of originality. How many great authors and poets of the past would, had they fallen into the hands of the present-day psychiatrist, have been trained as accountants and, like Dr. Johnson, found an escape from the horrors of unbridled thought and so deprived posterity of its priceless heritage? Furthermore, there is a possible danger in psychiatric guidance of maladjusted children and the placing of them in special schools. If, as Dr. Russell Brain and the writer of your leading article suggest, men are brilliant or perform brilliant works because they are unstable, the number of great men and women produced by the Welfare State will drop disastrously in the near future. If, on the other hand, the instability and peculiarities are secondary to the genius, the effect of psychiatry will be only transitory, and perhaps even slightly beneficial.

Finally, if the lessons learned in our researches are to be of value, the psycho-analyst should be intellectually equal to his subject, and the evidence must be, I repeat, reliable. Otherwise, though dog-latin labels appended to the mighty may fool many doctors and literary scholars, they will look somewhat unsuitable to him who has been privileged to study both these arts. —I am, etc.,

Bedwellty, Mon. R. A. HOEY.

SIR,—Dr. W. Russell Brain, in his stimulating paper on this subject (December 24, 1949, p. 1427), included Dostoievsky in the list of those writers who "were either insane in the sense that they would to-day have been regarded as certifiable, or, though perhaps never certifiable, were cyclothymes, schizophrenics, obsessionals, psychopaths, alcoholics, or drug addicts." In the case of Dostoievsky, who suffered from epilepsy, it should be of great interest to trace the effects of the writer's epileptic mental make-up upon his artistic creation.

Observations on a great many epileptics have conclusively shown that the physical discharge in form of fits is only part of the total picture of epileptic disease and that there exists a definite mental counterpart to the bodily phenomena. Its most striking features are antagonistic trends in the character of the epileptic with particularly marked display of religious and aggressive tendencies.

Before attempting to point to those qualities of Dostoievsky's work which seem most likely to be determined by his epileptic affliction, a short explanation of the dynamic factors involved in the formation of the epileptic character in general might be attempted. The periodic recurrence of loss of consciousness associated with epileptic attacks cannot fail to produce profound effects upon the mental state of these patients. There is ample evidence to suggest that the attacks give rise to an upsurge of unconscious death fear, reaching sometimes conscious level, and establish in time a kind of death complex that is mainly responsible for the operation and eventual consolidation of two utterly divergent trends in the character of the epileptic.

It is not difficult to understand the development of religious tendencies in the epileptic resulting from the ceaseless pressure exerted by his death complex. The preoccupation with our state of transitoriness is after all one of the deepest sources of religiosity in the non-epileptic too. It is more difficult to account for the origin of epileptic aggression. The aggressive act represents the most effective means of repudiating any sense of impending death. It is as though the process of intense self-assertion and harnessing of reserves of energy associated with it were felt by the epileptic as setting in motion vigorous counter measures to overcome the dreaded awareness of approaching death. Aggression, in my view, is the most reassuring answer to the overwhelming sense of annihilation experienced by the epileptic. The feeling of aroused vitality accompanied by it is perceived on his part as powerful refutation of any danger of his nearing end. Religiosity and aggression—two contradictory forms of reaction to neutralize the effects of specific traumatic experiences—fulfil their

purpose by liberating the epileptic from the paralysing influence of his death complex and enable him to achieve a certain measure of psychological equilibrium.

The fact that artificially induced epileptic attacks through electric-shock treatment can provoke changes in the character of patients may be looked upon as almost experimental evidence for the hypothesis of the moulding power of epileptic attacks. A case described by Russell Brain and E. B. Strauss[1] is quite illuminating in this respect. After the application of E.C.T., "a patient whom we treated for severe obsessional neurosis developed a form of religiosity quite foreign to his normal make-up."

The explanation given above may help understanding of the extreme dualistic features in the heroes of Dostoievsky's novels. Many of them represent a peculiar combination of criminal and saint. Raskolnikoff is a classical example of this strange mixture, being a murderer with saintly features. Several others could be mentioned. Their study confirms the belief that by invariably applying the principle of contrast in the character of his heroes Dostoievsky projected into his art what was primarily determined by his epileptic illness. In this manner the law governing the formation of the epileptic character transformed itself from a mere defence mechanism into an original and profound artistic principle—to the greatest benefit of mankind.—I am, etc.,

Cardiff. I. GROSSMAN.

REFERENCE

[1] *Recent Advances in Neurology and Neuropsychiatry*, 1945, London, p. 151.

Weil's Disease

SIR,—In your issue of December 17, 1949 (p. 1386), Dr. F. E. de W. Cayley describes a case of Weil's disease, referring particularly to certain biochemical tests for liver dysfunction. Some of the features, clinical and pathological, of the case are so unusual that to regard it as a typical example of this not uncommon infection would, I think, be misleading. I would like to refer to some of these unusual features, comparing them with findings in cases seen during the past year.

In the sixth decade of life Weil's disease is always a severe and frequently fatal condition. Invariably when it kills it does so by producing renal failure, and the severity of the infection can usually be deduced from the level to which the blood urea has risen. In this instance it is clear from the case notes that the illness was very severe. Deep jaundice and purpura are mentioned, both suggesting a virulent infection. It is surprising, therefore, to read that the blood urea was no higher than 35 mg. per 100 ml. and that the urine contained neither albumin, red cells, casts, nor excess of urobilin, though excess of the latter appeared later in the illness.

The demonstration of a marked excess of amylase in the serum not only indicates a pancreatic lesion but suggests that this was acute, widespread, and destructive. Ascites and pale stools support the suggestion. Such damage might result from a considerable interstitial haemorrhage within the pancreas, and, though there is no reason why a victim of Weil's disease, with its tendency to bleed, should not sustain such a catastrophe, we are told there was no abdominal pain. Acute haemorrhagic necrosis of the pancreas results usually in pain which is notorious for its severity. Furthermore, necropsies carried out in a dozen fatal cases have been remarkable in that massive bleeding into solid viscera, though it has been carefully searched for, has never been found.

The secondary rise of temperature, seen in about half the jaundiced cases, usually appears in the third week and not as in this case on the tenth day. Though the recurrence of fever, often referred to as "the after fever," may reach considerable proportions, it is unusual for it to persist for more than a week or ten days. In Dr. Cayley's case it lasted for over a month. Fever persisting in this way suggests a secondary infection and here was probably related to infection later shown to be present in the renal tract.

The results of agglutination tests differed from those I have met with in this type of case. In mild and moderately severe cases agglutinins can usually be demonstrated after the sixth day. In severe cases, however, it has been a constant observation that there is a marked delay in obtaining positive agglutination tests even at the lowest dilutions, and in a recent case, fatal on the tenth day of illness, the blood showed no agglutinins. It is therefore unexpected in a case of this severity to find that on the fourteenth day a positive test was obtained at 1:1000. The subsequent titre levels are also unusual, for instead of the rapid increase of titre we hear that on the twenty-third day no increase had been demonstrated, though by the thirtieth day 1:3,000 had been reached. In almost all cases of infection due to *Leptospira icterohaemorrhagiae*, as specific agglutinins develop co-agglutinins for *L. canicola* also appear and can be demonstrated in the blood, though in smaller amounts. Here, we are told, this was not the case.

Considerable uncertainty persists about the factors which contribute to the intense and characteristically brilliant jaundice which develops so rapidly in the severe examples of this illness. The histology of the liver in fatal cases is remarkable for the relatively intact state of the liver cells and the absence of necrosis as compared with that found in infective hepatitis. That haemolysis contributes to the jaundice is accepted, while blocking of smaller bile channels no doubt also plays a part. It is not surprising, therefore, that when the usual tests for liver function are applied unreliable and inconstant findings are obtained.

I have referred to the case notes relating to six patients seen during the past year. Three of these died. In these cases van den Bergh's test invariably gave very high readings when the quantitative method was applied. In one fatal case the bilirubin figure was 70 mg. per 100 ml. The serum alkaline phosphatase in no instance exceeded 14 units, and the average for the six cases was 9 units. In three the thymol turbidity and flocculation tests gave readings indicating liver-cell damage—in one fatal case turbidity was reported as 15 units and flocculation + + +. In the remaining patients results of the tests were well within normal limits. No help in prognosis was obtained from these tests.

In a personal communication Dr. J. C. Broom pointed out that in severe cases low figures for serum cholesterol are obtained and that a falling level may precede death. I have been able to confirm the former observation, and figures of 83 mg. and 104 mg. per 100 ml. have been obtained. It has not yet been possible to obtain serial figures.

Where the prothrombin content has been investigated it has been found to be reduced, being 45% in two cases. All these patients showed a marked excess of urobilinogen in the urine during the first ten days, though it disappeared later in a patient who survived.

No patient had a blood urea less than 110 mg. per 100 ml., and the three fatal cases showed figures well above 200 mg.; in one it was 440 mg. per 100 ml.

Though none of these patients showed any evidence of meningeal irritation when seen, five were submitted to lumbar puncture, and in all these an excess of cells, always above 100 per c.mm., was demonstrated, and the C.S.F. was bile-stained in all. Pleocytosis in bile-stained C.S.F. must usually indicate Weil's disease.

The history in Dr. Cayley's case is perfectly characteristic during the first week. Thereafter there appears so much that is unusual that it would not be wise to regard this as a typical example of severe Weil's disease; while to depend upon laboratory findings as recorded here might well mislead in the future. Finally, it cannot be too often repeated that jaundice is present in no more than half the cases in which leptospiral fever is due to *L. icterohaemorrhagiae* (Weil's disease), while it is quite exceptional in most of the other less common types of leptospiroses. In this country *L. canicola* is so far the only other leptospire which is known to produce disease in man.—I am, etc.,

Winchester. KENNETH ROBERTSON.

Diagnosis of Botulism

SIR,—The medical memorandum by Dr. David Kendall entitled "Recovery from Botulism". (November 12, 1949. p. 1094) emphasizes the importance of simultaneous epidemiological evaluation of a patient as an integral part of clinical evaluation. Much value of such a report is lost by failure to raise other diagnostic possibilities—viz., poliomyelitis.

With a family of three at risk in eating the "suspected meat," would it not be remarkable for only one parent to manifest botulism, one to escape, and the child to vomit for two days only after an interval of 24 hours after the suspect meal? Was not the child's case one of an expression either of (*a*) abortive

poliomyelitis, or (*b*) non-organic vomiting appearing at the height of the mother's vomiting, rather than "abortive botulism"?—I am, etc.,

New York. ALEX J. STEIGMAN.

Aureomycin in Treatment of Syphilis

SIR,—I was in Bagdad when Dr. Robert Lees's somewhat acrid letter (December 10, 1949, p. 1352) appeared concerning my paper (November 12, p. 1076) on the action of aureomycin on the dark-field positive lesions of early syphilis, and it was not seen by me until my return to the United Kingdom a short time ago. His criticism seems to be threefold: (1) the action of aureomycin was already known; (2) lack of planning; and (3) premature publication.

When I went to Southern Rhodesia at the end of April, 1949, the effects of aureomycin on syphilis were not generally known and indeed were quite unknown to me, even though I had recently made an exhaustive survey, containing over 230 references, of the previous year's literature on venereal diseases.[1] The pilot studies, however, which I had undertaken jointly concerning its action upon gonococcal and non-gonococcal urethritis[2] had made me resolve to find out for myself at the first opportunity.

The trials were commenced on May 18, 1949, and the paper was written at Zimbabwe during the latter part of June and revised under difficult writing conditions on July 8, when I was conducting a venereal diseases survey in a sparsely populated part of sub-tropical Africa. At this time I was of the opinion that the discovery was original, although I did not expect it would remain so for long. As I subsequently learned, Dr. Earle Moore made reference to his experiences at the Johns Hopkins Hospital (without, however, quoting chapter and verse) at a meeting held in London on May 31.[3] Travelling as I have been, the journals have been quite inaccessible to me over the last eight months.

The article appeared in the *British Medical Journal* on November 12, just over four months after it had been written. By this time Dr. Lees was able to say, "This was already known," although he did not advance any personal knowledge of the subject. It is somewhat ironic that had the publication been actually more premature than it was this criticism could not have been applied in such a manner.

The supply of aureomycin available for the study was limited to 48 capsules. The African is not amenable to follow-up attendance, and I was myself on the move. Under these circumstances it was planned that the study be confined to the immediate effects upon the dark-field positive lesions of early syphilis and be controlled by dark-field examinations—the only scientific method available. Even so nine persons were treated with this small amount, which is a greater number than other reported series.[4] At a later date two other patients were similarly treated, and the satisfactory initial results demonstrated to the Mashonaland Branch of the British Medical Association at Salisbury on October 11, 1949.[5]

Personally I have always felt that pilot studies are of immense value, as they give a lead as to whether more detailed tests based on prolonged observation are worth pursuing. In recent years Britain has lagged badly in the developments of the antibiotics for the treatment of venereal diseases, being apparently content to rely on the statements of our distinguished American colleagues. Desire or initiative to undertake a personal trial often seems to be lacking. In this case, there was nothing to be gained by withholding publication, for there was no further information possible to obtain.

It is agreed, even by Dr. Lees, that aureomycin has some action upon early syphilis, and I adhere to my contention that this discovery "opens up a new field of therapeutic investigation." It now remains for other venereologists to substantiate or refute this in a proper scientific manner rather than by premature deprecation in the medical press.—I am, etc.,

London, W.2. R. R. WILLCOX.

REFERENCES
1 *Bull. Hyg. Lond.*, 1949, **24**, 99.
2 *British Medical Journal*, 1949, **2**, 257.
3 *Brit. J. vener. Dis.*, 1949, **25**, 169.
4 *Proc. Mayo Clin.*, 1948, **23**, 574.
5 *Med. Pr.*, 1949, **222**, 585.

Medical Administrators

SIR,—Recent letters on medical administration have shown an all too common misunderstanding of the work of professional administrators.

No one, I think, would suggest that there is a profession of being a professor. You can only be a professor of some subject. The man who is an excellent professor of history would not necessarily have equal success as a professor of zoology. Similarly, there is no such thing as an administrator but only an administrator of something. You cannot administer any medical organization unless you are yourself trained in medical matters. The medical training alone is not sufficient: other qualities are necessary to the medical administrator in addition, but the professional training is primary and essential. The term "lay administrator" in relation to any professional matter is completely absurd and meaningless.

Perhaps a better analogy is that of the captain of a ship. All men with the technical ability to obtain a master's ticket do not necessarily have those other qualities which make them good commanders, but no one would dream of appointing a lay administrator to run the ship on the bare advice of a technically qualified captain. Technical competence plus a certain type of character and inborn flair make the technical administrator, but no amount of inborn talent will make an administrator of anyone without the technical knowledge.—I am, etc.,

Cambridge. C. G. EASTWOOD.

Euflavine in Epididymo-orchitis

SIR,—When I commenced using euflavine intravenously in 1934 the methods of treating gonorrhoea in males then in use gave somewhat unsatisfactory results. It was actually in an endeavour to speed up resolution of the gonococcal urethritis that this adjuvant procedure was adopted. Neutral euflavine must of course be used, 20 ml. of an 0.25% solution in distilled water being injected intravenously in the usual way.

Unfortunately it was found that this did not favourably modify the course of the urethritis. The injection was repeated weekly for, in some cases, several months without any apparent appreciable benefit. A total of 3,560 injections was given. In no case were any untoward side-effects, immediate or delayed, noticed. Using the above dosage, excretion of the euflavine is usually completed by, on the average, the third or fourth day. I append some notes on the use of euflavine by this method in certain conditions.

Gonococcal Epididymo-orchitis.—Although euflavine gave disappointing results in an uncomplicated case, we soon found that it produced quite remarkable results in epididymo-orchitis and/or prostatitis. A series of 170 cases of epididymo-orchitis was treated by this method. The accompanying pain disappeared in about four hours, the swelling rapidly subsided, and in all cases complete clinical resolution occurred after an average of four injections. By complete clinical resolution of the epididymo-orchitis is meant that careful examination by a trained V.D. worker would fail to show any abnormality.

In this series there were 83 patients with right-sided epididymo-orchitis who received 355 injections (average 4.28 each). Seventy-seven patients with left-sided epididymo-orchitis received 313 injections (average 4.06 each), and 10 patients with bilateral epididymo-orchitis received 40 injections (i.e., 4 each). In other words, resolution occurred, on the average, after four injections, irrespective of whether the condition was right- or left-sided or bilateral. I do not know of any other method of treatment which gives comparable results in gonococcal epididymo-orchitis. Similar excellent results are obtained in gonococcal prostatitis. Its use does not appear clinically to interfere with the action of penicillin, nor is it contra-indicated when the patient is also receiving neoarsphenamine—i.e., when a patient has gonorrhoea and syphilis.

If a patient presents himself with gonococcal urethritis and also epididymo-orchitis our practice is to give him one intramuscular injection of 200,000 units of penicillin, and at the same visit he receives an injection of 20 ml. of 0.25% neutral euflavine intravenously. The penicillin very rapidly clears up the discharge, but, as the epididymo-orchitis persists, the euflavine is repeated once a week until the epididymis is absolutely normal clinically. Then, of course, the usual tests of cure are carried out.

Urethral Stricture.—We have also since 1934 treated 24 cases of urethral stricture with euflavine intravenously in the same dosage

repeated weekly. We commenced with 10 ml. of 0.25% euflavine as a precaution, but found that excretion was practically normal in speed. We increased next to 15 ml., and if the euflavine had disappeared from the urine after three to four days we again increased the dose to 20 ml., and maintained this dosage. It should be noted that all these were cases of considerable severity—i.e., they were impassable to a 6/9 curved sound, this being established during diagnostic instrumentation. Without the use of sounds such as dilators they all gradually improved as regards micturition—difficulty of urination decreased steadily—and in the case of those who had an accompanying muco-epithelial discharge this rapidly vanished. Usually after eight injections the act of micturition was completed with such inconsiderable deviation from the normal that they were able to resume their work. One case, however, required 38 injections before being fit for discharge. Another case in this series has had to have repeated courses of injections but has been working throughout the treatment.

This method of treatment possesses obvious advantages over instrumental dilatation, especially from the patient's point of view, and except for the one case referred to none of the patients in the series has returned for a further course of treatment. Presumably in this series euflavine acts by allaying the inflammatory oedema which is found especially on the proximal side of the stricture. It has, of course, no effect on the stricture as such; nevertheless, after a course of injections as described it will be found that a 6/9 curved sound passes easily without any bleeding. It is probable that it is by allaying the inflammation on the posterior urethra and in the trigone that it permits of such remarkable results in epididymo-orchitis and prostatitis.

Other Conditions.—One young man of 18, who also was a congenital syphilitic, was referred to us with a tubercular left testis. (He also had pulmonary, meningeal, and renal tuberculosis.) His left testis appeared on examination to be on the point of breaking down and fistulating. We had to proceed with caution on account of the renal condition, so we commenced with an injection of 3 ml., increased to 5 ml. the following week, and so on up to 10 ml., given twice. The testis gradually improved, and instead of breaking down became "bone hard," probably from calcification. Except for its great weight and size it caused him no further trouble. It must not be assumed that I am recommending this form of treatment for tuberculosis of the testis. I have only indicated the factual result in this particular case; the man's medical officer considered that owing to his general condition he was unsuitable for operation.

I have not had the opportunity of trying this method of treatment in cases of bacilluria, except for one case which complicated pregnancy and in which it rapidly cleared up the condition. It would seem an obvious method to try in such cases on account of its safety and freedom from any side-effects.

I confidently invite others who are interested to try this safe and simple technique, especially in gonococcal epididymo-orchitis.—I am, etc.,

South Shields. D. J. MACKINNON.

The Natural History of Asthma

SIR,—I was very interested in Dr. D. H. Irwin's remarks on the psychogenic aspect of asthma (December 10, p. 1354) and would like to make some comments. He remarks on the parent–child tension which is invariably present, and he considers that "the effective parent in the relationship is usually the mother." I would say that the mother is emotionally stable until she is confronted by the bewildering and provocative personality with which her child is endowed. The increasing demands on the mother, which are telepathic rather than vocal, and the intelligent sensitivity, which is often overcompensated, keeps the mother constantly guessing and leads to a neurosis even in the most stable.

The evidence that the child is born with a specific personality pattern is fairly convincing. The uniformity of personality traits which is seen throughout Rogerson's[1] series, and in my own observations, indicates a common genetic denominator. Also, the asthma personality may be well developed long before the child ever has an asthmatic attack. The mother may, and usually has, already reared several sibs without any undue emotional tension; it is not true that only children occur more frequently in asthmatic groups.

With an asthmatic child a good mother responds by over-protectiveness, and it is necessary to curb this, perhaps, as Dr. Irwin suggests, by group therapy. If it is the child who is the primary source of the tension, by virtue of his specific personality pattern, then would it not be rational to treat the child, or preferably a group of children, in, say, a playroom? This has already been tried, of course, with notable success by Rogerson.—I am, etc.

London, E.15. L. E. WEAR.

REFERENCE

[1]Rogerson, C. H., *Quart. J. Med.*, 1937, **6**, 367.

Treatment of Wounded in Malaya

SIR,—I gather from my colleagues who served in the 1914–18 war that much of the surgical experience that was dearly bought in that war had to be gained all over again in the early years of the 1939–45 war. Those of us who served in the 1939–45 war hoped that the lessons learned would not be quickly forgotten. The Royal Society of Medicine, in convening the Inter-allied Conferences on War Medicine and in publishing these proceedings in book form, has done everything possible to ensure that the knowledge of war medicine gained should not be lost.

It is, therefore, all the more regrettable to learn from the reply by Mr. Shinwell to Mr. E. Hughes, concerning the number of surgeons in Malaya, that after less than five years so much has apparently been forgotten. The campaign in the Western Desert established the value of the field surgical unit and field transfusion unit being grouped at the main dressing station of a field ambulance with instructions to deal with "life and limb surgery." As a result of siting these units well forward, where they could deal with such cases as penetrating wounds of the abdomen and thorax and severe compound fractures of the femur, countless lives were saved. These casualties would have had little chance of survival had they been compelled to make the often tedious journey back to a C.C.S. or general hospital.

I appreciate that the problems of the jungle are not those of the Western Desert, but those of us who went from the desert to Sicily and Italy and later to Normandy found that the principles of forward surgical organization did not differ very greatly in the various theatres of war. It would appear from Mr. Shinwell's statement that there are only four Army surgeons in Malaya and Singapore Island. This number would seem quite inadequate to carry out the early surgical treatment which forms so important a part in war surgery. I sincerely hope that in a subsequent statement the Minister of War will be able to assure us that the medical services in Malaya to-day are no less efficient than in 1945; meanwhile his statement must give rise to the gravest misgivings.—I am, etc.,

Hove. REX BINNING.

With Whales and Seals

SIR.—While not unduly squeamish nor an opponent of blood sports as practised in this country—I follow hounds by car when I get the opportunity—I was nauseated when I read certain passages from Dr. H. R. Lillie's article entitled "With Whales and Seals" (December 24, 1949, p. 1467). If shortages are now so acute that human so-called civilization can only survive by the practice of such revolting cruelties on mammals that neither prey on man nor are vectors of any disease one wonders whether it is worth the while of medical science to strive towards the preservation of the fittest, let alone the unfittest.

A few days ago I read in a daily paper that a Whalemeat Advisory Bureau had been established in London. This announcement was alongside an advertisement depicting a housewife bearing a dish of whalemeat to her simpering family. The caption should have been, "Where ignorance is bliss." Why doesn't a protest come from the antivivisectionists and other individuals who take up their pens so readily on account of the indignities to which performing animals are subjected? Can it be that any of their own pampered pets are fed on whalemeat?

Slaughtering of whales and seals should be prohibited by international law until humane forms of killing have been devised and instituted. Commercial exploiters would then be stimulated to take rapid action.—I am, etc.,

Newcastle-upon-Tyne. E. T. EVERDELL.

POINTS FROM LETTERS

Health and the Soil

Dr. H. L. MACKINTOSH (Troon, Ayrshire) writes: McCarrison, Howard, and many others have demonstrated beyond reasonable doubt the very great importance of the quality of food to health and high resistance to disease, and that the quality of the food depends on a healthy active soil life, which in turn depends on an adequate supply of animal and vegetable organic matter in the soil. In other words the first factor of importance to the attainment of health is the health of soil on which our food is grown. Surely it is a matter for agriculture but not for medicine except indirectly. . . . The workers at the Peckham Centre in London have shown that in a cross-section of an average community 91% of the people suffered from disease, disability, or disorder of some kind or another. Most practitioners will be able to confirm these figures with little difficulty. In a small day-to-day survey of my own of the households which I was called to visit, 74% of the inmates were found to be suffering from some disorder or other, varying from head colds to heart disease, and probably if I had been able to examine the remainder the Peckham figures would have been reached with ease. . . . Real health and high resistance to disease depends not so much on a "health" service which has to do with already established disease but on the health of the soil and the treatment our food receives before it reaches us and on the existence of an economic system which will relieve the individual and family of chronic strain and provide all the other essentials of the healthy body and mind apart from high quality fresh food.

Scientific Society

Mr. JOHN DOBBING (London, S.E.24) writes: Bertrand Russell reaches the conclusion (December 10, 1949, p. 1307) that the first condition for a scientific society to be stable is that there should be a single government of the whole world "possessing a monopoly of armed force, and therefore able to enforce peace." I respectfully suggest that the expression "to enforce peace" is a contradiction in terms. The only kind of stability which can result from the "vast upheavals and appalling suffering" of future world wars, envisaged by Bertrand Russell as necessary preliminaries to a stable society, is the questionable stability enjoyed by our early ancestors; and, even if one could describe their state as a society, theirs was not the prosperity the majority of us would choose. Bertrand Russell admits that the lessons of experience become out of date as fast as they are learned. It is therefore quite possible that, although the vast upheavals and appalling suffering of the recent two world wars did not result in total annihilation, a third one may well do so. The fact that people throughout history have continually forecast that "the next war would be an annihilating one" and that their predictions have not in our experience materialized does not prove that quite soon it may not be possible to annihilate us all with another world war. We are drifting in that direction of our own volition, and we look to our great thinkers like Bertrand Russell not to allay our fears by means of his reassuring concluding remarks (which were as unjustified as any happy ending in an American film), but for leadership and guidance in saving ourselves by some means other than suicide. Reliance on armed force will be suicidal, as it has threatened to be in the past. . . .

Treatment of Rheumatic Fever

Dr. P. O. CROSSFIELD (Edinburgh) writes: With reference to Professor Hans Selye's experiments and hypothesis of adaptation syndromes (*Practitioner*, 1949, **163**, 393; *British Medical Journal*, 1949, **2**, 1129 and 1159), it is notable that the detrimental effect of mineralo-corticoids is inhibited by low sodium, low protein, and the production of acidosis. On the basis on his work, then, a relatively simple clinical trial of treating acute rheumatic fever with a low sodium diet, perhaps slightly reduced protein intake, and ammonium chloride in place of salicylates appears rational and worth while. The reduction of sodium intake in the diet could be achieved on the lines used in acute nephritis or congestive heart failure. The reduction of protein intake would, of course, have to be very guarded and perhaps even omitted, because of the negative nitrogen balance of acute rheumatic fever. The substitution of ammonium chloride for salicylates would, if successful, make the experiment more valid, especially if the pain of the joint lesions is relieved, since ammonium chloride is certainly not an anodyne and salicylates are believed to have anodyne properties. It may also show that the so-called specific effect of salicylates in rheumatic fever is mainly due to alteration in the alkali reserve. . . .

Antihistamine Drugs and the Common Cold

Dr. H. M. STANLEY TURNER (Brookwood, Surrey) writes: Many people who complain of "catarrh," "colds," and "constant colds" are sufferers from vasomotor rhinitis, which is definitely relieved by antihistamine drugs. May not this be how the confusion has arisen?

Obituary

CLIFFORD DOBELL, M.A., Sc.D., F.R.S.

The death of Clifford Dobell in London on December 23, 1949, has deprived the scientific world of an outstanding protozoologist, who in his brilliant studies of the intestinal amoebae of man made important and lasting contributions to tropical medicine.

Born in 1886, he was educated at Sandringham School, Southport, and at Trinity College, Cambridge. He graduated B.A. with first-class honours in the natural sciences tripos in 1906. In 1910 he proceeded to the M.A. and ultimately, in 1942, the Sc.D. While at Cambridge, Dobell studied zoology under Adam Sedgwick, continuing his training abroad—under Richard Hertwig at the Munich Zoological Institute, at the Zoological Station in Naples, and in Ceylon. In 1908 he was elected a Fellow of Trinity College. He was awarded the Walsingham Medal of the university, and he was a Rolleston prizeman, Oxford and Cambridge, and a Balfour student of Cambridge. Even as an undergraduate Dobell had begun to specialize in protozoology, and he wrote his first papers on the parasitic protozoa of lower animals in 1907; other publications followed devoted to protozoa, bacteria, and spirochaetes. In 1910 he was appointed assistant professor of protistology and cytology at the Imperial College of Science, London, a post which he held until 1919. There he continued his researches on the protozoa of lower animals, but the 1914–18 war turned his main interest to the human intestinal protozoa, and especially the amoebae. On this subject he soon became one of the foremost authorities in the world. When, in 1915, the War Office started a scheme for training protozoologists in the diagnosis of amoebiasis, Dobell was appointed to take charge of the classes which were held at the Wellcome Bureau of Scientific Research. From this period he devoted himself uninterruptedly to investigations of the intestinal protozoa of man. He was one of the first to demonstrate the existence and to appreciate the epidemiological significance of symptomless carriers of *Entamoeba histolytica*, whose number among the inhabitants of Great Britain he estimated at 10%. He standardized the methods of parasitological diagnosis of amoebiasis, revised the morphology and classification of the human amoebae, and played an important part in bringing about improvements in the treatment of amoebiasis with emetine. Such was the excellence of this work that in 1918—at the early age of 32—he was elected a Fellow of the Royal Society.

In 1919 he published his classic monograph, *The Amoebae Living in Man*. This book, though written thirty years ago, is still an indispensable source of accurate information for all serious workers in tropical medicine. Dobell became protistologist to the Medical Research Council at the National Institute for Medical Research in the same year, and there he remained till his death. His next work of medical importance was *The Intestinal Protozoa of Man*, published in 1921. Originally conceived as a joint work with, and bearing the name of, F. W. O'Connor, it was actually written entirely by Dobell. This book provided a valuable practical guide to all the intestinal protozoal infections. At that time the complete life histories of the human amoebae were still unknown. The discovery by Boeck and Drbohlav in 1925 of suitable culture media enabled Dobell to carry out a series of remarkable investigations, published under the general

title "Researches on the Intestinal Protozoa of Monkeys and Man." In these papers, which appeared between 1928 and 1943, Dobell not only described the full life-cycle of all but one (*Iodamoeba*) of the human amoebae, but also established their identity and interchangeability with those of macaque monkeys. Apart from these contributions to medical knowledge, Dobell wrote numerous papers of zoological interest, and made many contributions to the history of protozoology, including his masterpiece *Antony van Leeuwenhoek and his Little Animals.*

Clifford Dobell carried out all his investigations with painstaking thoroughness, while his published works were always perfect in literary style and bore the mark of wide erudition and scholarship. By nature he was retiring, shunning the limelight, and content to devote all his time to scientific and literary pursuits in the seclusion of the laboratory and the study. But he was always ready to share his encyclopaedic knowledge with those who sought his advice. He was respected universally and admired by many, though a few were resentful of his outspoken criticisms. Many of us will remember him as a loyal and generous friend.

Dobell belonged to many scientific and medical societies at home and abroad, and served at various times on a number of committees. He married in 1937 Monica Baker, who was the step-daughter of his old friend, the late Dr. William Bulloch, F.R.S.—C. A. H.

W. H. NEWTON, M.D., D.Sc.

Dr. W. H. Newton, who was appointed professor of physiology in the University of Edinburgh in March, 1948, died on December 20, 1949, at his home in Edinburgh. He was 45 and at the height of his powers as a teacher, as an administrator, and as a research worker.

William Henry Newton was born in 1904 at Spalding, in Lincolnshire, where his father was minister. The family moved to Harrogate, and he went to Ashville College, and later to Manchester University. There he graduated M.B., Ch.B. in 1929, proceeding M.D. in 1934. Previously he had taken the B.Sc. in physiology with first-class honours in 1925, going on to the M.Sc. a year later. The atmosphere must have been stimulating. H. S. Raper had just succeeded A. V. Hill in the chair of physiology at Manchester, and B. A. McSwiney and G. L. Brown were on the staff. Newton collaborated with McSwiney for a time in work on the effect of *p*H on smooth muscle, but in 1930 he was appointed Sharpey Scholar, and joined the staff of University College, London, under Professor Lovatt Evans. A year later he married Stella, the daughter of Robert Reynolds; they had two daughters.

Newton soon established himself as a stimulating teacher and a fluent and attractive writer. Apart from his work as senior lecturer at University College, he was visiting lecturer at St. George's Hospital and at the Chelsea Polytechnic. He succeeded Lovatt Evans as the author of *Recent Advances in Physiology*, and was responsible for the fifth, sixth, and seventh editions, rewriting most, or all, of the book each time. He worked with G. F. Marrian on the combined effects of oestrogens and oxytocin on the uterus, and gradually became a leading authority on the physiology of pregnancy. In 1937 he went with a Rockefeller Fellowship to work with Professor Edgar Allen at Yale, and he contributed a chapter to Allen's book, *Sex and Internal Secretions.* He returned to London just before the war, and when the war took Lovatt Evans away he acted as head of the department at University College. He was one of the secretaries of the Physiological Society from 1942 to 1947, and a member of the editorial board of the *Journal of Physiology.*

In 1944 Newton became professor of physiology at Liverpool, and there he worked on relaxin, perfected an apparatus for studying the metabolism of pregnant mice, wrote a useful *Introduction to Physiology*, and greatly improved the department. He moved to Edinburgh in 1948, and soon won the affection and admiration of his colleagues. In his last illness he endured several months of increasing pain with great fortitude, upheld by the courage and skilled nursing of his wife. He will be remembered by all who knew him as a friendly person who concealed great gifts behind an unassuming manner. It was surprising to find that some of the beautiful water-colours in his home were his own work. His early death robs physiology of one who had accomplished much and would have accomplished much more.—J. H. G.

HENRY CORSI, M.B., F.R.C.S.

Dr. Henry Corsi, who was for many years physician to St. John's Hospital for Diseases of the Skin, died suddenly in Switzerland on January 1 at the age of 56. Henry Corsi was born in London and educated at Rugby, Pembroke College, Cambridge, and St. Bartholomew's Hospital. He took the Conjoint diploma in 1918, the F.R.C.S. in 1921, and he graduated M.A., M.B., B.Ch. in 1926. Towards the end of the 1914–18 war he was house-surgeon to Mr. Girling Ball, as he then was, in the military wards of St. Bartholomew's Hospital. Subsequently he was resident surgical officer at the Miller Hospital, Greenwich, and still later he became surgeon to the London Lock Hospital. Not long after this he became interested in dermatology, and acted as chief assistant to Dr. Adamson and later to Dr. Roxburgh in the skin department at St Bartholomew's Hospital. Finally, after some 16 years as chief assistant, he was made assistant physician to the department. Meantime he had given up his appointment at the Lock Hospital and had become physician to St. John's Hospital for Diseases of the Skin. Owing to ill health Dr. Corsi did not feel able to continue his work at St. Bartholomew's and at St. John's Hospitals, and he therefore resigned from the former some five years ago. In the last year or two he had been chairman of the medical committee of St. John's Hospital and president of the St John's Hospital Dermatological Society. He was a member of the British Association of Dermatology and Syphilology and of the Section of Dermatology of the Royal Society of Medicine. He was honorary secretary in 1934 of the Section of Dermatology at the Annual Meeting of the B.M.A. His published papers were few in number, but each represented a great deal of careful work. The most important of them were concerned with the therapeutic value of the gold compounds, the *x*-ray treatment of epithelioma of the skin, and the use of thorium X.

Henry Corsi had a most lovable personality. A loyal and trustworthy colleague, he nearly always turned up early at the hospital in order to get on with the work. No matter how many people were asking him to do things at the same time, he remained suave and imperturbable. His work was always done most conscientiously, even when he was suffering considerable pain from an old injury to his hip. His dry humour was much appreciated by those who knew him well, and he made admirable after-dinner speeches. As chairman of his hospital committee he was most successful and a favourite with all who knew him. During the recent war his home at 114, Harley Street, was often a refuge for "blitz-displaced persons," who could always be sure of a welcome and a bed in his hospitable basement. Henry Corsi's parents were Italian, and he

spoke that language as well as he spoke English, but he had also mastered French and German, and his linguistic ability proved most useful to the abstracting section of the *British Journal of Dermatology*. Corsi had a fine library. He was a great student of Dante and had several editions of *La Divina Commedia*, and he liked reading Goethe's *Faust* in the original. He was very fond of mountains and ski-ing, and generally managed to visit Switzerland or Italy for two or three weeks several times a year. It was on one such expedition that he was taken suddenly ill and died on New Year's Day. He leaves a son and daughter, to whom the sympathy of all who knew him will be extended.

J. P. BUCKLEY, M.D., M.S., F.R.C.S.

Mr. J. P. Buckley, who was for many years on the honorary staff of the Manchester Royal Infirmary, died on December 20 at his home in Manchester.

John Philip Buckley was educated at Rugby and at Trinity College, Cambridge, where he took first-class honours in the natural sciences tripos in 1904. He took his M.A. in 1908, the year in which he qualified, after a period at Manchester and at the London Hospital. He took his F.R.C.S. in 1911 and proceeded M.D. and M.S. in 1912. He was associated with the Manchester Royal Infirmary right from the start of his career, as a house-surgeon there and as medical officer in charge of the Central Branch. He was also on the staff of the Salford Royal Hospital before being appointed honorary surgeon to the Manchester Royal Infirmary. He served as a captain in the R.A.M.C. in the 1914–18 war, and on returning to Manchester he was appointed lecturer in surgical pathology at the University.

Among other appointments, Mr. Buckley was consulting surgeon to the Manchester Ship Canal Company and visiting surgeon at the Grangethorpe Ministry of Pensions Hospital. He contributed a number of articles to this and other journals, almost all of them on some aspect of abdominal surgery, in which he was principally interested. There must be many men who served as surgical dressers on the old S.2 Unit who will remember Philip Buckley as a most approachable chief, who was always interested in student activities. He was a capable lecturer, but he was perhaps at his best at the bedside or in the lively small tutorial groups which he liked to conduct in the wards or in the theatre.

We are indebted to Professor E. D. Telford for the following appreciation : Philip Buckley was in every sense a big man, and owed his outstanding physique and brain to his father, who in the latter half of the nineteenth century was well known in Manchester as a surgeon, a *bon vivant*, and a friend of Edwin Waugh. Philip was educated at Rugby, and of this school he always spoke with affection. His medical training began at Trinity College, Cambridge. Always a keen sportsman, at first well known in Rugby Union circles, he later became a skilled player of rackets and tennis, and continued to play a notable game up to the day of his death. He was a first-rate surgeon, with good hands and technique, his special interest lying in the anatomy and treatment of femoral hernia. I was associated with him in the running of a large surgical unit for twenty-two very happy years, during which all work, pleasant and unpleasant, was shared impartially without ever a question as to who had this bed or that. He was a great favourite with students, to whom his witty talks made a ready appeal. He was in much request as a speaker and was equally at home in the serious discourse of a medical society and in the joking cut-and-thrust of an after-dinner speech. Latterly he devoted much time to medico-legal work, in which his wide knowledge and strong common sense carried him far. But he may by some be best remembered in his library at home, showing to his friends treasures collected with loving care by his father and himself. Those of us who worked with Philip at the Royal Infirmary feel that we have lost a good friend and a most lovable man.

NEIL MacVICAR, M.D., D.P.H., LL.D.

Dr. Neil MacVicar, who was medical superintendent of the Victoria Hospital, Lovedale, South Africa, for thirty-five years, died on December 2, 1949, in Johannesburg. When he retired in 1937 Sir Edward Thornton, then Secretary for Public Health, said that he had perhaps done more than anyone else in South Africa to promote the health of the Bantu people.

Neil MacVicar was born in 1871 at Manor, near Peebles, in Scotland, where his father was parish minister. On leaving school he was apprenticed to a firm of lawyers in Peebles. He developed, however, an intense interest in the peoples of Africa, which led him to interview many men with African experience, among them H. M. Stanley. As a result he decided to become a medical missionary. On completing his legal apprenticeship he entered Edinburgh University as a medical student, and graduated M.B., C.M. with first-class honours in 1894. He took the D.P.H. in 1902, and proceeded M.D. in 1907. After qualifying he held house appointments at Edinburgh Royal Infirmary, and in 1896 he was appointed medical officer to the Blantyre Mission of the Church of Scotland in Africa. While there he studied malaria, blackwater fever, and smallpox, in one epidemic carrying out upwards of 30,000 vaccinations with the aid of African assistants whom he had trained.

In 1900 Dr. MacVicar returned to Scotland, and after a further period of study was appointed medical officer to the Victoria Hospital, Lovedale, taking up his duties there in 1902. The hospital had been opened in 1898, and subsequently closed during part of the Anglo-Boer War. MacVicar therefore started from scratch, and during the ensuing thirty-five years, by unremitting labour and wise administration, he saw the hospital grow to a total complement of 170 beds. From the beginning MacVicar was impressed by the ignorance of the Bantu people in matters of hygiene. Therefore, in addition to gaining their confidence in the hospital, he set himself the great task of promoting health education. In 1903, in face of strong opposition from both European and Bantu sections of the population, he began the training of Bantu girls as nurses. The success of his work may be judged by the hundreds of Bantu girls who are to-day practising or training as nurses throughout the Union. In 1905 he started writing on the subject of medical training for the Bantu, and, although he was able to make a beginning with a health class at Lovedale Missionary Institution in 1909, it was not until 1941 that he saw his dream come true when the University of the Witwatersrand opened its doors to Bantu medical students. In 1909 he also founded the South African Health Society, and he remained editor-in-chief of its journal, *The Health Magazine*, until shortly before his death.

In the midst of these labours Dr. MacVicar found time to make a number of contributions to the medical literature. His studies on tuberculosis in the South African native, on scurvy and malnutrition, and on the influence of Bantu domestic and economic circumstances on the incidence of disease made him a leading authority on these subjects for many years. In 1940 he was present at the opening by

the Hon. H. G. Lawrence, then Minister of Public Health, of the MacVicar Tuberculosis Hospital at Lovedale, which stands to-day as a lasting memorial to his work. A further well-deserved honour came to him in March, 1945, when the University of the Witwatersrand conferred on him the degree of Doctor of Laws, *honoris causa*.

MacVicar's character was many-sided. With a deep humility of spirit he combined tenacity of purpose. With a wide understanding of human nature at its worst and weakest, he had yet a great faith in his fellow-men, and especially his African fellow-men. His zeal for his work never flagged. During his service in Africa, Neil MacVicar married Miss Jessie Samuels, a nursing sister, who was his constant helper until her death in 1936. He is survived by his son and daughter, both graduates in medicine of his old university.—S. A. S.

J. E. LOVELOCK, B.M., B.Ch., M.R.C.P.

Jack Lovelock, the world-famous Olympic miler and former world mile record holder, was killed in New York on December 28, 1949, when by accident he fell under a subway train. Lovelock, who was only 39, had been working at the Manhattan Hospital, and because he felt ill he was returning to his home in Brooklyn.

A New Zealander and a student at Otago University, John Edward Lovelock came to Oxford as a Rhodes Scholar and took his B.A. in 1934. He graduated B.M., B.Ch. in 1937 as a student at St. Mary's Hospital, and he took the M.R.C.P. in 1940. He was a house-physician and subsequently medical registrar at St. Mary's Hospital, and he also had a period as a house-physician at the Brompton Hospital. Later he was appointed director of the rehabilitation department at St. Bartholomew's Hospital. During the war he was for a time on the staff of the E.M.S. hospital at Mill Hill, and later served as a major in the R.A.M.C., which he had joined in 1941. Dr. Lovelock married his American wife in 1945, and two years later he settled in New York and became assistant director of physical medicine and director of rehabilitation at the Manhattan Hospital for Special Surgery in New York. In recent years he had been particularly interested in the treatment of cases of poliomyelitis.

Jack Lovelock first became prominent in athletics while an undergraduate. He ran the record "mile of the century" in 4 min. 7.6 sec. at Princeton, New Jersey, in 1933. He was known everywhere as "the perfect miler," and he ran his races at an even, rhythmic pace which wore out his opponents. His great ambition was to win the Olympic 1,500 metres in Berlin in 1936, and this he did. His time then of 3 min. 47.8 sec. was a world record and is still the Olympic record. At different times he lost several races to S. C. Wooderson, but it was said that after 1932 he never lost a race that he really wanted to win. In 1934 he won the Empire Games Championship, and after his Olympic victory two years later he retired from the track. Since then he had written and broadcast on athletics, and he had acted as honorary coach at the A.A.A. summer school. As recently as last summer he was one of the officials at a match between the combined Oxford and Cambridge athletics team and Princeton and Cornell Universities.

Since his tragic death was announced many tributes have been paid to Lovelock as an athlete and a sportsman. Many of them echo the comment of Lord Burghley, president of the Amateur Athletic Association: "Jack Lovelock was not only a magnificent athlete but he also had the wonderful gift of making friends wherever he went."

Dr. ANNA JUSTINA AUGUSTA WILSON died on November 28 in St. Mary's Hospital, Paddington, after a long and trying illness. She was believed to be about 86. She was born in India, and her father was an Army officer who later took holy orders and became the vicar of Wilton in Yorkshire. The earlier part of her life was spent in India, at first with her father and later with her brother, who was collector of Ootacamund. When her brother was attached to the staff of Lord Wenlock, the governor of Madras, she lived for a time in Government House, where she was immensely popular, famous for her beauty and her social attainments. She would return from tiger shooting or hunting at Ootacamund to write gay social paragraphs for the *Times of India* or else to delight the assembled company with Chopin recitals. Incidentally, all her three brothers were killed in the Boer War, which elicited a letter of sympathy from Queen Victoria. In India she married Mr. P. R. Wilson, a well-known banker of Bombay, but her marriage did not diminish her restless energy. She started to study physical medicine, going to Sweden first, because that country led the world in this subject at the time. While with the Swedes she added a knowledge of their language to her already perfect French and German. Back in London Justina Wilson opened a school, "The Swedish Institute," in Cromwell Road, and soon was training large numbers of physiotherapists. This school she later transferred to her niece, Mrs. Guthrie-Smith, and it is now a part of St. Mary's Hospital. She also took charge of the physiotherapy department at St. Bartholomew's Hospital, and between running her school and this department she found time to study at the Royal Free and to qualify in medicine—at the age of 53. Qualification produced a problem at St. Bartholomew's and Dr. Wilson had to leave. She then started a new department at St. Mary's Hospital. Working under the most primitive conditions in the basement, she soon built up a busy and efficient department. She also took the Cambridge D.M.R.E. in 1920. Still this was not sufficient to keep her fully occupied, and she sat for the membership at 61 and for the Fellowship of the College of Physicians of Edinburgh at 65. From then on she developed a busy private medical practice. The keynote of this practice was her vigorous treatment, and she could mobilize in turn all the resources of physiotherapy, allopathy, and homoeopathy to help the patient. But it was really her own determination and stimulating personality which seemed to effect cure. It was as if her patients were afraid to do other than get well, and it was hardly surprising that her clientele included some of the best-known names in the land.

During the war Dr. Wilson fell in the black-out and fractured her pelvis. For two months she was in bed, but this did not deter her. Soon, in a small bedroom, she arranged the necessities of her practice, and patients arrived and were interrogated and examined by the bedside. Finally, from a sterilizer by her bed she would produce a syringe, and, with a parting shot from this, speed the patient on his or her way with a final invocation, "Mind you get well," or, "Come back cured." This fall unfortunately resulted in an osteoporosis of the spine, so that she lost stature and her head became very bent, but still her work went on until her husband died in February, 1948. Then the vital spark was quenched and she longed for the day when she would join him in his grave on the Sussex Downs. This came about in the presence of a group of her friends and relatives on the afternoon of December 2. As the coffin was lowered one noticed that no age was engraved upon the lid: she had kept this secret to the last.—A. D. W.

Dr. EDWARD HUGHES JONES died at his home in Rhyl on December 3 at the age of 84. A student at the University of Edinburgh, he graduated M.B., C.M. in 1890, proceeding M.D. in 1909. After a short period as an assistant in Dowlais, South Wales, Dr. Jones settled in Rhyl in 1893, and continued in practice there for over 55 years, retiring only in 1948. He was for many years senior surgeon to the Royal Alexandra Hospital and the Prince Edward War Memorial Hospital at Rhyl, and he acted as medical officer of health for the Rhyl urban and rural areas.

Dr. John Jones writes: As one who had abundant opportunity of knowing him, may I be permitted to pay a sincere tribute to the qualities and virtues of this talented member

of our profession, which rightly earned for him the deep respect and affection of his patients. He had a strong sense of duty, and the promptitude with which he responded to urgent calls was commendable. His mental endowments were of a high order, which, combined with gentle, skilful hands and a rich experience, made him remarkably successful in his profession: many will cherish his memory with gratitude. Though not outwardly a very religious man, he had a deep faith, and daily read his Bible.

H. L. D. writes: To complete the admirable tribute to LANCELOT BROMLEY'S career by "W. E. T." (December 31, 1949, p. 1532), as a student at Guy's he was a member of the hockey eleven which for three years in succession won the Inter-hospital Cup, and he also played for Sussex during those years. As a student, too, the unfailing neatness of his written work distinguished him from most of his fellows. I find it hard to realize that he has gone.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

The Council of the Senate has gratefully accepted the bequest to the University by the late Mr. Walter Jowett of the sum of £5,000 for research into diseases of animals, especially those transmissible to man and tropical diseases of domestic animals.

Drs. Harry Butler and Michael Harty have been reappointed University Demonstrators in Anatomy for five years from October 1, 1949, and January 1, 1950, respectively; and Drs. Ivor William Broomhead and David Henry Morgan Woollam have been appointed University Demonstrators in Anatomy for three years from January 1, 1950.

In a Congregation held on December 10, 1949, the degree of M.D. was conferred on H. R. E. Wallis (by proxy) and M. H. K. Haggie (in person).

UNIVERSITY OF LONDON

The following lectures have been arranged at University College, Gower Street, W.C.: January 16, 23, and 30, at 4.30 p.m., Professor R. A. Morton, "Biochemistry of Carotenoids"; January 20 and 27 and February 3 and 10, 5.15 p.m., Dr. F. Bergel, "Aspects of Pharmacological Chemistry"; February 7, 14, and 21, at 5.15 p.m., Dr. L. C. Thomson, "Visual Physiology"; February 23, 1.15 p.m., Dr. J. Joseph, "The Human Thumb"; February 23 and March 2 and 9, 4.45 p.m., Dr. T. S. G. Jones, "The Peptide Bond in Biochemistry"; February 27 and March 6 and 13, at 5.30 p.m., Professor J. Neyman (University of California), "Statistical Problems Connected with Medical Diagnosis"; March 9, 10, and 13, at 5.30 p.m., Professor B. Rensch, "Zoology." Admission to all the above lectures is free, without ticket.

A special University Lecture on "The Circulation in Disease" will be delivered by Dr. J. G. G. Borst, Professor of Internal Medicine in the University of Amsterdam, at Westminster Medical School (Meyerstein Lecture Theatre), Horseferry Road, London, S.W., on Tuesday, February 7, at 5 p.m. Professor P. Grabar, of the Pasteur Institute, Paris, will deliver a special University Lecture on "Origin and Functions of Globulins and Antibodies" at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., on Monday, January 23, at 5.30 p.m. The lectures are addressed to students of the University and to others interested in the subjects. Admission is free, without ticket.

EPIDEMIOLOGICAL NOTES

Poliomyelitis in 1949

The publication of the Registrar-General's weekly return for the week ended December 31, 1949, makes it possible to estimate the figures of incidence and mortality for the whole year with fair accuracy. Corrected figures of notifications and the number of deaths for the whole of England and Wales for 1949 are not yet available, and in the following table those for the last quarter have been estimated from the figures of uncorrected notifications and from the weekly returns of deaths in the Great Towns. The years 1926 and 1938 have been included in the table because they had the highest recorded incidences up to 1947.

England and Wales

Poliomyelitis and Polio-encephalitis Notifications and Deaths in Years

	1926	1938	1947	1948	1949
Notifications ..	1,297[1]	1,585[1]	7,766[2]	1,859[2]	5,800[3]
Rate per 100,000 ..	3	4	18	4	13
Deaths ..	235	256	707	241	600[3]
Rate per million ..	6	6	16	6	14

[1] Uncorrected. [2] Corrected. [3] Estimated on the assumption that the ratios $\frac{\text{"corrected" notifications}}{\text{"uncorrected" notifications}}$ and $\frac{\text{Deaths in Great Towns}}{\text{Deaths in England and Wales}}$ were the same in the fourth quarter as they were in the third quarter.

The epidemic of 1949 was second only to that of 1947 and considerably exceeded those of pre-war years. As in 1947 distribution was widespread, but in contrast to 1947 the incidence was relatively high in the South-West and relatively low in the North-East.

Typhoid in S.S. Mooltan

In all, some 45 members of the crew of the s.s. *Mooltan* are now in hospital, and the diagnosis of typhoid fever has been confirmed in 30. Examination of specimens of stools has demonstrated also five ambulant excretors of *S. typhi*. In passengers 8 cases have occurred (one each from Northern Ireland, Scotland, Lowestoft M.B., Oldham C.B., Shrewsbury M.B., Sunderland C.B., Twickenham M.B., and Wandsworth M.B.).

The dates of onset of the illness in those cases about which details are available suggest that the source of infection arose during the last three weeks of the voyage, and persisted until the vessel docked in the Port of London on December 15, 1949. Chloramphenicol is proving of value in the treatment of these cases.

Discussion of Table

In *England and Wales* during the fortnight reviewed there were decreases in the notifications of scarlet fever 439, acute pneumonia 100, and acute poliomyelitis 53, with increases in the incidence of measles 88 and dysentery 88.

The largest falls in the notifications of scarlet fever occurred in Lancashire and London, where the cases notified were 88 and 48, respectively, fewer than in the preceding week. In the first week reviewed an increase of 132 in the notifications of measles was reported in Durham, followed by a fall of 114 in the second week. The local trends of whooping-cough showed only small variations.

Notifications of dysentery are now at the highest level for over a year. The chief outbreaks during the fortnight were Glamorganshire, Penarth U.D. 30 and 43; Northumberland, Newcastle-upon-Tyne C.B. 7 and 26; Yorkshire West Riding, Barnsley C.B. 11 and 15; Yorkshire East Riding, Kingston-upon-Hull C.B. 16 and 2.

In *Scotland* the only significant variation in the notifications of infectious diseases was that of acute primary pneumonia, with an increase of 103 in the first week followed by a decrease of 94. The incidence of dysentery remained high; almost half the cases were notified in Glasgow.

In *Eire* the fall in the incidence of measles was continued, and the notifications of scarlet fever declined to a half of the level of a month earlier.

In *Northern Ireland* a rise of 37 and a fall of 49 were recorded for the notifications of measles during the two weeks. Londonderry County was the only area where the incidence of measles has increased in both weeks. The fall in the incidence of scarlet fever was continued, and the notifications in Belfast declined by 49 and 35.

Week Ending December 31

Notifications of infectious diseases in England and Wales during the week included: scarlet fever 2,327, whooping-cough 1,018, diphtheria 102, measles 1,978, acute pneumonia 842, cerebrospinal fever 22, acute poliomyelitis 61, dysentery 197, paratyphoid fever 2, typhoid fever 28.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended December 17. [No. 50

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1949					1948 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever ..	37	2	17	3	1	35	5	23	3	1
Deaths		—	2				—	1		
Diphtheria	92	14	31	5	4	124	9	36	11	5
Deaths	1	—	—	—	—	—	—	—	—	—
Dysentery	197	13	75	—	2	54	8	46	2	1
Deaths				—	—				—	—
Encephalitis lethargica, acute	—	—	—	1	—	—	—	—	—	—
Deaths		—					—			
Erysipelas			38	10	4			38	4	2
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				18					40	
Deaths	23	1	5	3		33	2	7	5	1
Measles*	1,793	34	37	57	156	9,800	180	80	60	37
Deaths†			—	—	—			1	—	—
Ophthalmia neonatorum	31	—	8	—	—	58	2	6	—	—
Deaths										
Paratyphoid fever ..	8	1	—	—	—	1	1	1(A)	—	—
								1 (B)		
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal ..	676	38	15	4	14	1,082	67	12	7	1
Deaths (from influenza)‡	41	5	—	—	—	24	2	—	—	—
Pneumonia, primary ..			390	33				451	37	
Deaths	252	40		14	11	292	67		8	6
Polio-encephalitis, acute	6	2				1	—			
Deaths										
Poliomyelitis, acute ..	87	9	1	1	1	28	2	2	—	—
Deaths§	6	1				3	1			
Puerperal fever		—	5				—	4		—
Deaths										
Puerperal pyrexia‖ ..	73	6	3	1	3	95	12	7	1	—
Deaths		—					—			
Relapsing fever ..	—	—			—	—	—			—
Deaths										
Scarlet fever	2,829	190	245	89	226	1,426	64	288	173	42
Deaths†			—	—	—			—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	5	—	—	2	—	7	2	1	2	—
Deaths	—	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough* ..	984	32	66	26	58	2,471	154	178	62	14
Deaths	—	—	—	—	—	6	—	—	—	—
Deaths (0–1 year) ..	281	30	44	20	11	325	44	52	34	10
Deaths (excluding stillbirths)	5,607	838	699	187	144	5,326	891	646	195	129
Annual death rate (per 1,000 persons living)			14·0	11·6				13·0	12·2	
Live births	6,711	1066	861	244	196	7,196	1158	1011	305	219
Annual rate per 1,000 persons living ..			17·3	15·1				20·4	19·1	
Stillbirths	189	25	23			193	23	25		
Rate per 1,000 total births (including stillborn)			26					24		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a Summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended December 24. [No. 51

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1949					1948 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever ..	28	—	10	—	1	22	—	13	—	1
Deaths		—	1				1	1		
Diphtheria	81	15	25	1	3	100	6	32	7	11
Deaths	—	—	—	—	—	3	—	—	—	1
Dysentery	221	16	67	1	4	30	5	28	—	3
Deaths				—	—				—	—
Encephalitis lethargica, acute	1	—	—	—	—	—	—	1	—	—
Deaths		—					—			
Erysipelas			28	6	3			54	6	1
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				27					28	
Deaths	27	1	1	4	2	28	2	8	—	2
Measles*	1,684	32	23	47	107	8,959	110	86	29	50
Deaths†			—	—	1			1	—	1
Ophthalmia neonatorum	35	2	7	—	—	18	1	3	—	—
Deaths										
Paratyphoid fever ..	5	1	2(B)	—	—	3	—	—	—	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal ..	634	29	7	4	7	792	35	2	9	1
Deaths (from influenza)‡	27	5	2	2	2	25	2	2	—	—
Pneumonia, primary ..			296	22				337	23	
Deaths	296	44		18	9	258	51		7	10
Polio-encephalitis, acute	10	—				2	—			
Deaths										
Poliomyelitis, acute ..	71	8	2	2	—	17	2	1	1	—
Deaths§	5	—				2	—			
Puerperal fever		—	3				3	—		—
Deaths										
Puerperal pyrexia‖ ..	72	6	7	1	1	78	7	5	1	1
Deaths		—					—			
Relapsing fever ..	—	—			—	—	—			—
Deaths										
Scarlet fever	2,416	142	221	81	176	1,154	42	246	120	40
Deaths†			—	—	—			—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	3	—	—	1	1	4	1	1	2	1
Deaths	1	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough* ..	936	39	63	42	44	1,791	100	130	66	8
Deaths	3	—	—	1	—	16	1	—	1	1
Deaths (0–1 year) ..	337	43	42	48	12	315	42	47	16	8
Deaths (excluding stillbirths)	5,712	862	701	255	149	4,854	738	551	158	110
Annual death rate (per 1,000 persons living)			14·1	15·8				11·1	9·9	
Live births	6,569	1015	877	326	204	6,263	992	766	239	200
Annual rate per 1,000 persons living ..			17·6	20·2				15·5	15·0	
Stillbirths	177	23	24			175	28	18		
Rate per 1,000 total births (including stillborn)			27					23		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

Medical News

Royal Society Appointments

The president of the Royal Society has appointed the following vice-presidents for the ensuing year. Treasurer: Sir Thomas Merton. Biological Secretary: Sir Edward Salisbury (director of the Royal Botanic Gardens, Kew). Physical Secretary: Sir David Brunt (professor of meteorology at the Imperial College of Science and Technology). Professor C. E. Tilley (professor of mineralogy and petrology in the University of Cambridge).

Mapother Bequest

The Medical Research Council invites applications for a research fellowship in psychiatry to be provided from a fund established by the late Dr. and Mrs. Edward Mapother. The fellowship will be awarded by the Council to a suitably qualified graduate for whole-time work on the histochemistry of the nervous system. It will be carried out under the direction of Professor A. Meyer and Dr. H. McIlwain at the Institute of Psychiatry (University of London), Maudsley Hospital, Denmark Hill, London, S.E.5. Candidates should preferably have had experience in the use of both biochemical and histological methods. The award will be made for one year in the first instance and be renewable annually over a period of three years in all. Stipend will ordinarily be at the rate of £600 per annum, but may be fixed at a higher rate up to a maximum of £800 per annum, and provision of up to £200 per annum will also be made by the council for research expenses. Applications, giving particulars of age, qualifications, previous career, and research experience, together with the names of two referees, should be lodged with the Secretary, Medical Research Council, 38, Old Queen Street, Westminster, London, S.W.1, not later than January 31.

Research into Deafness

The trustees of the Alexander Pigot Wernher Memorial Trust, through the Medical Research Council, have established a Research Unit on Deafness at the Institute of Laryngology and Otology, University of London. Dr. T. S. Littler has been appointed director of the unit, with Miss E. Whetnall as assistant director. The unit has also the assistance of Dr. D. B. Fry, consultant in phonetics to the Institute, and a staff of registrars, physicists, and technicians. The unit is housed at the Golden Square Hospital, where it will work in close association with the Deafness Aid Clinic of the Royal National Throat, Nose, and Ear Hospitals. Its programme of research includes an investigation into the possibilities of improved treatment of otitis media and the study of deafness developing with age. Methods of measurement of residual hearing for adults and children and the various problems associated with the use and design of hearing-aids are also being studied. The unit has agreed to carry out research on behalf of the Electro-acoustics Committee of the Medical Research Council and the Ministry of Health. In collaboration with the Deafness Aid Clinic it is studying the design of the bone-conduction and insert receivers and associated plastic mouldings.

Films for Children

The British Medical Students Association held a series of film shows for children during the week before Christmas in a number of London hospitals. The experiment proved to be very successful, and a more ambitious programme is planned for next Christmas.

"Science To-day"

The weekly newsletter *Science To-day* surveys recent advances in science, both biological and physical, and is intended for the non-specialist. It now appears as a small magazine between covers, and the first number of the New Year includes accounts of an antithyroid substance found in plants of the genus *Brassica* (which includes cabbages and turnips) and of electrical measurements of nervous impulse. It is edited by Mr. A. W. Haslett, M.A., 104, Clifton Hill, London, N.W.8 (35s. a year).

Sims Commonwealth Travelling Professorship

The Royal College of Physicians has nominated Professor D. M. Dunlop, professor of medicine in the University of Edinburgh, as Sims Commonwealth Travelling Professor for 1951. He will visit Australia and New Zealand in the summer of that year.

Wills

Professor Major Greenwood, professor emeritus of epidemiology and vital statistics in the University of London, left £18,024; Dr. Francis Hernaman-Johnson, physician to the Charterhouse Rheumatism Clinic, left £713; Dr. James Ferguson, formerly medical officer of health for Surrey, £7,011: Dr. William Drake Copplestone, of St. Martin, Jersey, £50,528: and Dr. Christopher Thackray Parsons, of Havant, Hants, £27,981.

COMING EVENTS

Lecture-demonstrations on Neurology and Psychiatry

A series of lecture-demonstrations on neurology and psychiatry began at St. George's Hospital Medical School, Hyde Park Corner, London, S.W., on January 12 and will be continued on Thursdays, at 4.30 p.m., until March 30. The lecture-demonstrations are open, without fee, to all medical practitioners and senior medical students.

Meeting of Registrars

A meeting of the South-west Region Registrars Group will be held at the Hawthorns Hotel, Woodland Road, Clifton, Bristol, on Tuesday, January 17, at 8.15 p.m.

London School of Hygiene and Tropical Medicine

Professor N. H. Swellengrebel, director of the Department of Tropical Hygiene, Royal Institute for the Indies, Amsterdam, will deliver two lectures at the London School of Hygiene and Tropical Medicine (Main Lecture Theatre), Keppel Street, Gower Street, W.C., on Tuesday and Wednesday, January 17 and 18, at 2 p.m. On January 17 he will discuss "Plague in Java" and on January 18 he will describe how the malaria service in Indonesia came into being. All interested are invited to attend the lectures.

St. John's Hospital, Lewisham

Dame Barrie Lambert will open the extension of the nurses' home at St. John's Hospital, Morden Hill, Lewisham, London, S.E., on Friday, January 20, at 3 p.m.

Royal Institute of Public Health and Hygiene

Dr. George Graham has been appointed Harben Lecturer of the Royal Institute of Public Health and Hygiene for 1949. His subject is "Diabetes." The lectures will be given on January 23, 24, and 25, at 3 p.m. each day. They will be delivered in the lecture hall of the Institute, 28, Portland Place, London, W.

Society for Endocrinology

The Society for Endocrinology has arranged a lecture on "The Nature of Adrenocorticotropic Hormone (ACTH)" to be given by Dr. C. H. Li (Institute of Experimental Biology, University of California, Berkeley, California) at the Royal Society of Medicine, 1, Wimpole Street, London, W., on Thursday, January 26, at 5 p.m. Admission is free, without ticket.

Public Health and Industrial Health

The Royal Institute of Public Health and Hygiene announces that courses of instruction, both whole-time and part-time, will commence as follows: January 27, Diploma in Public Health (for those holding the C.P.H.); February 17, Diploma in Industrial Health (Part 2); and March 24, Certificate in Public Health and Diploma in Industrial Health (Part 1). Full details may be obtained from the secretary of the Institute, 28, Portland Place, London, W.

SOCIETIES AND LECTURES

Friday

MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, Maida Vale, London, W.—At Medical School, January 13, 5 p.m., demonstration of Neurosurgical Cases by Mr. Valentine Logue.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—January 13, 8 p.m., dissertation by Mr. I. B. Tait.

WEST KENT MEDICO-CHIRURGICAL SOCIETY.—At Miller Hospital, Greenwich High Road, London, S.E., January 13, 8.30 p.m., clinical meeting.

Saturday

S.E. METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Farnborough Hospital, Farnborough, Kent, January 14, 10.30 for 11 a.m., "*The Management of the Chemotherapy of Tuberculosis*," by Dr. D. G. Madigan.

Monday

HUNTERIAN SOCIETY.—At Mansion House, London, E.C., January 16, 8.30 p.m., "*The Early Diagnosis of Gastric Carcinoma*," Hunterian Lecture by Professor René-A. Gutmann (Paris).

UNIVERSITY COLLEGE, Gower Street, London, W.C.—January 16, 4.30 p.m., "*Biochemistry of Carotenoids*," by Professor R. A. Morton.

Tuesday

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—January 17, 5 p.m., "*Histopathology of the Skin*," by Dr. I. Muende.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, Keppel Street, Gower Street, W.C.—January 17, 2 p.m., "*Plague in Java*," by Professor N. H. Swellengrebel (Amsterdam).

MIDDLESEX COUNTY MEDICAL SOCIETY.—At West Middlesex Hospital, Isleworth, January 17, 3 p.m., general meeting. "*Non-specific Mediastinal Adenitis*," by Dr. E. P. Quibell; "*Potassium Metabolism in Intestinal Disease*," by Dr. P. M. McAllen.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—January 17, 5 p.m., "*The Diagnosis and Management of Hirschsprung's Disease*," Arris and Gale Lecture by Mr. F. Douglas Stephens.

Wednesday

HARVEIAN SOCIETY OF LONDON.—At 11, Chandos Street, Cavendish Square, London, W., January 18, 8 p.m., annual general meeting. "*Some Reflections on General Medical Practice in the last 30 Years*," Presidential Address by Dr. Desmond MacManus.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—January 18, 5 p.m., "*X-ray Technique*," by Dr. C. W. McKenny.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, London, S.E.—January 18, 4.30 p.m., lecture-demonstration for postgraduates by Dr. E. Stengel.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, Keppel Street, Gower Street, W.C.—January 18, 2 p.m., "*How the Malaria Service in Indonesia Came into Being*," by Professor N. H. Swellengrebel (Amsterdam).

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—January 18, 5 p.m., "*The Surgical Aspects of Renal Damage in Childhood: Assessment, Salvage, and Aftermath*," Arris and Gale Lecture by Mr. D. F. Ellison Nash.

ROYAL MICROSCOPICAL SOCIETY, B.M.A. House, Tavistock Square, London, W.C.—January 18, 5.30 p.m., annual general meeting. 6 p.m., "*Chemically Induced Derangements of Cell Division*," Presidential Address by Dr. R. J. Ludford.

Thursday

BRITISH INSTITUTE OF RADIOLOGY.—At 32, Welbeck Street, London, W., January 19, 8.15 p.m., Ordinary Meeting followed by Joint Meeting with Radiological Section, Royal Society of Medicine. "*Use of Radioactive Isotopes—Some Diagnostic Techniques*," papers by Mr. N. Veall, B.Sc., Mr. C. P. Haigh, and Dr. M. Reiss, and Professor J. Rotblat, D.Sc.

EDINBURGH CLINICAL CLUB.—At B.M.A. Rooms, 7, Drumsheugh Gardens, Edinburgh, January 19, 8 p.m., "*The Home Management of the Tuberculous Patient*," by Professor Charles Cameron.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—January 19, 5 p.m., "*Tumours of the Ovary*," Erasmus Wilson Demonstration by Dr. Magnus Haines.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At 26, Portland Place, London, W., January 19, 7.30 p.m., "*The Malaria Epidemic of 1943–6 in North Holland*," by Professor N. H. Swellengrebel (Amsterdam). A discussion will follow.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—January 19, 4.30 p.m., "*Neurology*," lecture-demonstration by Dr. Denis Williams.

WESTMINSTER HOSPITAL SCHOOL OF MEDICINE, Meyerstein Lecture Theatre, Horseferry Road, London, S.W.—January 19, 5.30 p.m., clinico-pathological meeting, discussion: "*Pulmonary Mycosis*."

Friday

BRITISH ASSOCIATION OF PHYSICAL MEDICINE.—At St. George's Hospital, London, S.W., January 20, 5 p.m., "*Some Modern Methods in Chest Surgery*," by Mr. A. H. M. Siddons.

BRITISH INSTITUTE OF RADIOLOGY.—(1) At 32, Welbeck Street, London, W., January 20, 5 p.m., meeting of medical members. (2) At Royal Society of Medicine, 1, Wimpole Street, London, W., January 20, 8.15 p.m., Joint meeting with Radiological Section, Royal Society of Medicine, continued. "*The Therapeutic Uses of Radio-isotopes*," speakers Dr. Ralston Paterson, Dr. Warrington, Dr. R. J. Walton, Mr. Sinclair, and Mr. C. J. L. Thurgar.

BRITISH TUBERCULOSIS ASSOCIATION.—At 26, Portland Place, London, W., January 20, 3.15 p.m., "*In the Opinion of This Meeting Infection, Though Necessary, is Not the Major Factor in the Prevalence of Tuberculosis*," debate in which Drs. H. J. Ustvedt and Lionel Houghton will speak in favour of the resolution and Drs. Peter Edwards and Alice Stewart against it. Dr. J. B. McDougall will also take part in the discussion.

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., January 20, 2.15 p.m., "*Adnexal Tumours*," by Professor R. McWhirter.

MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, Maida Vale, London, W.—At Medical School, January 20, 5 p.m., Neurological Demonstration by Dr. W. Russell Brain.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—January 20, 8 p.m., "*The Handicapped Child*," by Mr. D. W. MacLean.

SOCIETY OF CHEMICAL INDUSTRY: FINE CHEMICALS GROUP.—At Burlington House, Piccadilly, London, W., January 20, 6.30 p.m., Joint meeting with Food Group. "*Fine Chemicals and the Food Industry*," by Professor A. C. Frazer.

UNIVERSITY COLLEGE, Gower Street, London, W.C.—January 20, 5.15 p.m., "*Aspects of Pharmacological Chemistry*," by Dr. F. Bergel.

Saturday

BIOCHEMICAL SOCIETY.—At British Postgraduate Medical School, Ducane Road, Hammersmith, London, W., January 21, 11 a.m., 283rd meeting.

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Central Middlesex County Hospital, Park Royal, N.W., January 21, 2.30 p.m., clinical meeting.

YORK MEDICAL SOCIETY.—At 17, Stonegate, York, January 21, 8.30 p.m., "*Intestinal Obstruction*," by Professor Ian Aird.

APPOINTMENTS

BOWEN, JOHN WALTER M.B., B.Ch., D.P.H., C.P.H., Medical Officer of Health, Abertillery Urban District Council, and Medical Officer of Health Blaina and Nantyglo Urban District Council (Divisional Medical Officer for these areas); Schools Medical Officer, Divisional Education Area, Monmouthshire County Council; and Assistant County Medical Officer.

MOSELEY, J. H., M.B., Ch.B., M.R.C.P., Consultant Paediatrician to the Portsmouth Area and the Isle of Wight.

ROCHE, G. K. T., M.B., B.S., D.A., Consultant Anaesthetist, Royal National Orthopaedic Hospital, Great Portland Street, London, W.

ST. THOMAS' HOSPITAL, London, S.E.—*Consultant Anaesthetists*: J. D. Laycock, M.B., B.S., D.A., R. B. Wright, M.B., B.Chir., D.A.

WEIR, J. H., M.D., D.P.H., B.Hy., Medical Officer of Health, Royal Borough of Kensington and Metropolitan Borough of Chelsea.

WHITTLES, JAMES HILL, M.D., D.P.H., Deputy Medical Officer of Health of Rochester and Chatham, and Assistant County Medical Officer of Health for Kent.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Divers.—On December 18, 1949, to Betty (née Craig), wife of Dr. Lloyd Divers, a daughter.

Elsom.—On January 1, 1950, at Lichfield, to Joyce (née Grant), wife of Dr. A. R. Elsom, a son.

Gough.—On December 22, 1949, at Longmead, Spade Oak Reach, Bourne End, to Clara Lee (née Burgess), M.B., Ch.B., wife of Dr. C. W. C. Gough, a daughter.

Jeanes.—On November 30, 1949, at Woolwich Memorial Hospital, to Joyce (née Johnson), wife of Dr. C. W. L. Jeanes, a daughter, Rosemary Anne—a sister for David.

Laycock.—On November 18, 1949, at Hargeisa, British Somaliland, to Winifred Gladys (née Worth), wife of Handley T. Laycock, F.R.C.S., a daughter—Pamela Athene.

Stewart.—On January 2, 1950, at Oldchurch Hospital, Romford, to Evalyn (née Linscott), M.B., D.O.M.S., wife of John Marshall Stewart, M.B., D.M.R.D., a daughter.

Vowles.—On December 25, 1949, to Mary (née Knowles), M.B., Ch.B., wife of Keith D. J. Vowles, M.B., Ch.B., a son.

MARRIAGES

Richards—Winter.—On December 26, 1949, at Catford, London, S.E., Harold J. Richards, M.B., B.S., F.R.C.S., D.A., only son of William J. Richards, The Square, Pembury, Carms, to Josephine P. Winter, M.B., B.S.

Solomons—Edgar.—On November 22, 1949, in London, Bethel Solomons, jun., M.D., M.R.C.P.I., of Dublin, to Gillian Edgar, of Hambleden, Buckinghamshire.

DEATHS

May.—On December 22, 1949, at Brynsworthy, Westerham, Kent, Percival Marshall May, M.R.C.S., L.R.C.P., Surgeon Captain, R.N., Ret.

Stephen.—On December 14, 1949, at Ashford Hospital, Middlesex, George Stephen, M.B., F.R.C.S.Ed., of 28, Leigham Drive, Isleworth, Middlesex, aged 46.

Studdert.—On November 19, 1949, Augustine Fitzgerald Studdert, L.R.C.P.&S.I., of Bellmullet, Co. Mayo, aged 77.

Waring.—On December 18, 1949, at Nottingham, John Alfred Waring, M.B., aged 83.

Warren.—On December 9, 1949, at Rocky Hill House, 19, London Road, Maidstone, Kent, Frederick William Warren, L.R.C.P.&S.I., L.M., aged 79.

Webb.—On December 10, 1949, at the Royal Sussex County Hospital, Frederick Henry Webb, M.B., Ch.B., of Halfway House, Rottingdean, Brighton, aged 50.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Local Analgesia in Obstetrics

Q.—*Could you tell me how to effect local analgesia by procaine infiltration in the second stage of labour? I understand that local analgesia is becoming an established practice for forceps delivery in cases with cardiac complications.*

A.—Local analgesia is becoming increasingly popular for low forceps delivery and is eminently suitable for those cases where there is negligible mechanical difficulty and where the indication for the operation is maternal ill-health. The method is efficient and is practically free from risk to either mother or child; it does not interfere with uterine action or the physiology of the third stage of labour, and it allows other procedures, such as episiotomy or the repair of perineal incisions or tears, to be undertaken. The following method combines features from several of the many techniques described. Procaine in either 0.5 or 1% solution in saline is usually employed, and the total amount should not exceed 120 ml. of the weaker or 60 ml. of the stronger solution. Indeed, experienced operators rarely use more than 60 ml. of 0.5% solution. With the patient in the lithotomy position, a weal is raised at a point midway between the anus and ischeal tuberosity on one side. The adjacent tissues, in particular the line of a proposed episiotomy incision, are infiltrated. With a finger in the vagina (some operators prefer the rectum in order to ensure that the bowel is not punctured) the ischeal spine is identified and a long needle is guided from the original weal up to the spine. About 10 ml. of procaine solution is then injected around the spine and in the area between it and the inner aspect of the ischial tuberosity. This blocks the pudendal nerve as it passes round the spine and comes forwards to reach Alcock's canal. The needle is then redirected parallel to the lateral wall of the vagina, and the levator ani muscle together with the fascia above and below it is infiltrated. Finally the needle is passed forward subcutaneously through the labium majus to the mons veneris and solution is injected along its tract to interrupt cutaneous branches of the ilio-inguinal and of the small sciatic nerves. The opposite side of the vulva is then treated in like manner. The accompanying diagram showing the arrangement of the nerves and the sites of injection is taken from an article by Griffin and Benson (*Amer. J. Obstet. Gynec.*, 1941, **42**, 863); however, the easiest method of learning the technique is to see a practical demonstration. The usual error of a beginner is to concentrate too much on the superficial tissues, whereas well-placed injections around the pudendal nerves and the levatores ani are the essentials, and, indeed, except for the site of the episiotomy, there is hardly any need for subcutaneous infiltration. It takes at least five minutes for the injections to become really effective, and operative procedures should not be started too soon. Moreover, gentleness is essential; rough handling or strong and sudden traction will destroy the patient's confidence.

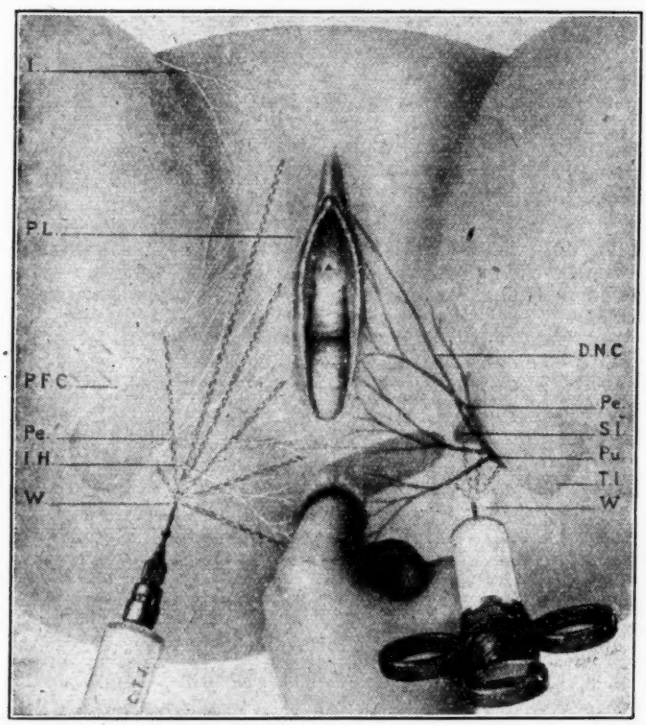


Diagram showing local infiltration technique of the nerves of the female perineum. Superficial and deep innervation is shown on the right and left side of the patient, respectively. I., ilio-inguinal nerve; P.L., posterior labial nerves; P.F.C., posterior femoral cutaneous nerve, perineal branch; Pe., perineal nerve; I.H., inferior haemorrhoidal nerve; D.N.C., dorsal nerve of clitoris; Pu., pudendal nerve; S.I., spine of ischium; T.I., tuberosity of ischium; W., intradermal weal. (Reproduced by courtesy of the Editor of the *American Journal of Obstetrics and Gynecology*.)

Migraine Treated by Pituitary Hormone

Q.—*I have seen reports that migraine has been successfully treated by a pituitary hormone or by A.P.L. Is this a sound method of treatment? Is it safe, and can you give me details of dosage? Where can I find references in the literature?*

A.—Migraine is a little-understood disorder, and the relative failure of specific therapy is indicated by the number of remedies suggested from time to time, all of which are accepted with enthusiasm because of the distressing character of migraine and then usually fall into disuse or are classified as "ameliorative in some cases." Among recent remedies, carbachol, 2 mg. (1/30 gr.) by mouth, repeated if necessary within a few hours, is an alternative to ergometrine. It is a derivative of choline and a parasympathetic stimulant. Progressively increasing doses of neostigmine by mouth have also been recommended; and the same applies to injections of histamine in increasing doses for desensitization in that group of migraine sufferers who show a positive histamine intracutaneous response.

Migraine does appear to have some relationship to pituitary–ovarian function. It may be worse near or during a menstrual period or at the climacteric, and may disappear during pregnancy. Nevertheless, it may be equally distressing and specific in the male. Because migraine is sometimes associated with a small pituitary fossa—a condition which may be present without symptoms—it has been suggested that it is due to a tendency of the pituitary gland at times to enlarge within a restricted encasement. Pituitary hormone, or A.P.L., has been recommended by Moffat (*J. Amer. med. Ass.*, 1937, **108**, 612) and by Leyton (*Lancet*, 1942, **1**, 488). No convincing explanation of the rationale of this treatment is given, and its use in a large series of cases, with controls, is essential before this therapy can be accepted. If there is any rationale, it might be based on the principle that the administration of any hormone tends to depress the activity of the gland which secretes the hormone given. The writer is not personally impressed by the evidence yet put forward in favour of A.P.L. treatment, and does not consider that the evidence justifies acceptance of this treatment as being specific or reliable. The dosage recommended in the reports is 200 to 300 units once or twice weekly.

Insulin Shock and Electric Convulsion Therapy

Q.—*Generally speaking, how long should strict observation be continued in hospital, and subsequently at home, in cases treated by insulin shock therapy and those treated by electric convulsion therapy? Can both types of treatment be repeated and, if so, after what interval?*

A.—Patients who have been treated by insulin shock would be fit to leave hospital a couple of days after the termination of treatment, if their mental state warrants it. There is no late shock or other undesirable sequel to be expected after that. Electric convulsion therapy (E.C.T.) causes a disturbance which lasts only about an hour. Patients are commonly given this

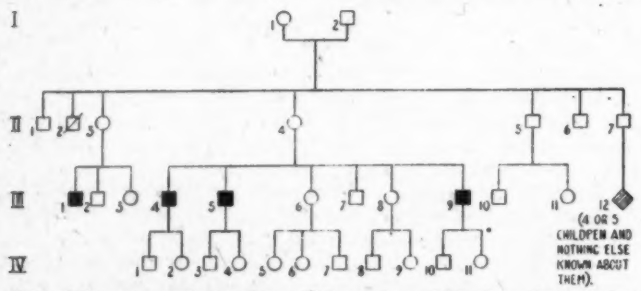
treatment in out-patient clinics, and are afterwards taken home by a responsible relative, but they are able to go to work next day.

Both types of treatment can be repeated—that is to say, in each case a second course can be given at a very short interval. It all depends on how much treatment the patient has had. When a patient has received a course of 40 or 50 treatments by insulin coma it is unusual for further treatment to be necessary for a number of months or years—that is, until there is a genuine relapse. In the case of E.C.T., treatment might have to be continued after a comparatively short interval of a few days or weeks, but the total number of treatments given in fairly close succession should be limited to a comparatively small number. After about twelve treatments E.C.T. tends to have a bad effect on the memory.

Inheritance of Retinitis Pigmentosa

Q.—*The mother of a boy of 6 years has inquired about the chances of the child's developing retinitis pigmentosa, as three of her brothers and a cousin developed this condition between the ages of 30 and 40. The pedigree, so far as information is obtainable, is as shown below. The method used is that suggested by Fraser-Roberts in his book "Medical Genetics." Could you kindly give some indication of the chances of IV 7 developing this condition?*

A.—There are two possible explanations for the transmission of retinitis pigmentosa shown in this excellent pedigree: the gene may be sex-linked or recessive. That two sisters should have affected children, all four of them boys, rather strongly favours the first hypothesis. If so III 6 has a one-in-two chance of carrying the gene herself, and if she does so the chance that she has passed it on to IV 7 is also one in two; the chance that the latter will develop the disease is therefore one in four.



I 1 and 2 was a cousin marriage; II 5 wore very thick glasses but was not considered to have retinitis pigmentosa; III 2 is 35 years old and is not affected; III 7 is 40 and not affected; III 10 is 35 and not affected; III 6 is the inquirer; IV 7 is the child in question; II 2 died at the age of 20.

On the other hand, recessive transmission, though not so likely, is by no means impossible. Given a recessive gene, the probability of getting four affected boys, two normal boys, and three normal girls in the two sibships is not particularly small. The chance that two sisters should both have happened to marry carriers of the gene is much smaller. Against this low probability must be set the fact that recessive retinitis pigmentosa is much commoner than the sex-linked type. If inheritance is recessive, the chance that IV 7 will develop the disease is negligible. The mother could be told that one of two types of inheritance is involved. If the inheritance is of one kind the chance is very small indeed—less than 1 in 100; if it is the other type—and unfortunately this is rather more likely—the chance is one in four. Incidentally, the cousin marriage in generation I is a red herring in this instance and has no bearing on the interpretation.

Fragilitas Ossium

Q.—*Is there any treatment for fragilitas ossium congenita? If thymus gland is indicated, what are the details of administration?*

A.—There is no curative treatment for osteogenesis imperfecta or fragilitas ossium. The suggestion by Secord (*Proc. Mayo Clin.*, 1936, **11**, 1) that there may be some possible value in thymus-gland extract has not been confirmed. This group of cases of disordered bone development is dependent on a "chemistry of genetics." Like some other unfavourable genetic influences, it may vary in intensity of expression and effect even in the several affected members of a family, and may also in some reveal a tendency to slow spontaneous improvement, especially with fragilitas ossium. Whilst fragilitas ossium has nothing to do with nutritional deficiency, it should be recognized that an associated avitaminosis D in such a case would seriously aggravate the tendency to fractures. This is well illustrated in the case recorded by Snapper (*Medical Clinics on Bone Diseases: A Text and Atlas*, 1943, New York), in which a negative calcium balance was converted to a positive balance by 12,000 units of vitamin D per day, this being accompanied by a disappearance of limb pains

NOTES AND COMMENTS

Stainless Steel Dentures.—Mr. N. J. AINSWORTH (Director of Prosthetics, Royal Dental Hospital) writes: Under the heading "Any Questions?" (November 26, p. 1246) an otherwise excellent answer to a question on the use of stainless steel dentures is marred by a mis-statement. It is not true to say that "powerful and expensive presses are necessary to mould it to the shape of the jaw." Such presses are in common use, but an equally good result is possible in the hands of a skilled mechanic using the same methods as are used for the shaping of wrought gold plates, only greater care and time are required and possibly three metal dies and counterdies instead of two. Further, if stainless steel is used, as the questioner seems to imply, as a surface to a plastic plate this combination is readily achieved and gives the ease and closeness of adaptation of a plastic material and the hardness and strength of stainless steel. It remains true, of course, that the acrylic plastics are quicker and simpler to make, better in appearance and therefore much more popular though less durable, but the incorrect though widely held belief to which I have drawn attention is responsible for the undeserved neglect of a most valuable dental material.

Surgical Dexterity.—Dr. THOMAS GIBSON (Torquay) writes: In your recent obituary notice of the late Professor T. P. McMurray (November 26, p. 1236), Sir Harry Platt mentions an incident in which McMurray displayed his wonderful dexterity with the scalpel. Reading this, my memory recalled a somewhat similar incident, which I witnessed as a student at the Edinburgh Royal Infirmary in the early 'nineties of the last century. The theatre was crowded with spectators, including, as on the Liverpool occasion, a number of visiting surgeons, who had come to see Thomas Annondale, the dapper little professor of clinical surgery, perform some big operation. "Tommy" was remarkably expert with the knife, and he also dearly loved showing off. So, before starting the big operation he arranged, as a sort of curtain raiser, to do a quite simple operation, namely the removal of an adenoma from a woman's breast. With one incision he went through skin, subcutaneous tissue and capsule, shelled out the tumour with his hand, tossed it into the air, caught it like a cricket ball, and then smilingly bowed to his astonished audience. The whole thing was done in a flash, and might be described as a piece of surgical jugglery. I confess that while I vividly remember this trivial operation I have clean forgotten what the big one was.

Corrections

In the first leading article in the *Journal* of January 7 there was an unfortunate misprint (p. 62). A reference to the work of "Fields and Woods" should, of course, have read "Fildes and Woods."

Describing WHO fellowships in the *Journal* of December 10, 1949 (p. 1363), we said that full details about them can be obtained from the General Secretary at Geneva. We understand that inquirers should write to the Ministry of Health, Whitehall, London, S.W.1, and not to the General Secretary.

In the news paragraph headed "Treatment of Anthrax, Botulism and Snake-bite" (December 31, 1949, p. 1537) the telephone number of the Nottingham City Hospital, Hucknall Road, Nottingham, should have been given as 66292 and not 42554.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone. Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.
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